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A CASE OF HYPOPHYSEAL TUMOR WITH ASSOCIATED TUMOR-LIKE ENLARGEMENT OF THE PARATHYROIDS AND ISLANDS OF LANGERHANS[1]

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The literature abounds in cases which present clinically the so-called pluriglandular syndrome associated with various tumors or other lesions of the endocrine organs, notably the hypophysis. Far less frequent, however, are the cases in which multiple distinct anatomical lesions are found in several of these organs simultaneously. A case recently autopsied here presents certain unique features in this respect which make it worthy of recording, not because of the changes themselves, but because of their hitherto undescribed coincidence, and their suggestion of correlation of the endocrine glands.

Briefly, the combination of lesions to be described consists in a large inoperable tumor arising in the region of the hypophysis, associated with multiple tumor-like nodules of the parathyroid glands and of the islands of Langerhans in the pancreas. This combination has not been described in the literature, nor has it occurred in the 10,000 autopsies performed in this department, although similar lesions have been found separately in each of these organs.

Tumors of the hypophysis are of course relatively frequent, those arising within the gland itself,—usually in the anterior lobe,—being more common than those arising from the hypophyseal duct or from other extrahypophyseal epithelial primordia. In Cushing's series (1) of twenty-nine proven cases of pituitary tumor, twenty-three were of the former variety, *i.e.*, homoplastic, while six were heteroplastic. Of the homoplastic tumors, the neutrophilic or chromophobe type is by far the most frequent. In acromegaly one usually but not invariably finds a tumor composed largely of eosinophile cells, and in rare instances the basophile cells are found to predominate. The

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majority of the heteroplastic tumors arise from some epithelial remnant of the hypophyseal duct and have for the most part the characteristic architecture of an adamantinoma. A small number of tumors arising outside of the gland, however, appear to be identical with many of the homoplastic tumors and probably develop from some embryonic rest of hypophyseal tissue, possibly in a diverticulum of the duct. In the series of 10,000 autopsies there were thirty-two cases of pituitary tumor, not including cysts. Of these, twenty-five arose within the gland, six in the duct, and one resembling a hypophyseal adenoma was situated above the gland, which itself was normal. Five of the twenty-five tumors of the gland proper showed the typical changes of acromegaly. Of the total of thirty-two cases, complete autopsies were performed in only nineteen, including all the acromegalics.

In none of the nineteen cases, nor in any of those found in the literature, were any special lesions present in the pancreas. A few gave what was little more than a suggestion of hyperplasia of the islands of Langerhans, the islands being numerous and occasionally somewhat enlarged, but not really abnormal. No tumor-like nodules of the islands were seen.

In one of the above mentioned cases of acromegaly two out of three parathyroids found were definitely enlarged, each measuring 12 by 6 by 4 mm. and showing microscopically a simple hyperplasia. This recalls a case of acromegaly described by Erdheim (4), in which four enlarged parathyroids were found, the largest measuring 17 by 6 by 3 mm. These showed in part the normal parathyroid architecture, but also a few vaguely outlined areas in which the nuclei were smaller and the cells more numerous. A similar case has been reported by Claude and Baudouin (11). In none of the other cases of hypophyseal tumor encountered were any parathyroid changes noted.

The records concerning changes in the adrenals, thyroid, and glands of reproduction, associated with pituitary tumors, are conflicting and unsatisfactory, so that no definite conclusions can be drawn. In eight of the nineteen cases in the autopsy series the genitalia were infantile in type. In three cases cysts of the ovary were found, but these were without special significance. The testicle in one case showed a complete absence of the interstitial cells of Leydig; in

another the Leydig cells were abundant but vacuolated and apparently degenerated. The adrenals in the majority of cases were normal, but in two instances the adrenal medulla was considered hyperplastic, in one case hypoplastic.

More than a dozen tumors of the parathyroids have been described, the first by De Santi (2) in 1900 and others by Benjamins (3), Erdheim (4), Hulst (5), MacCallum (6), Weichselbaum (7), Harbitz (8), Thompson and Harris (9). Most of these were accidental discoveries at autopsy, occurring usually in a single parathyroid, and varying from 2 to 4 cm. in diameter. A few were larger, notably that described by Benjamins, which was said to be the size of a child's head. Microscopically, the tumors have shown a wide variation in morphology. Some have presented solid masses of eosinophile cells or of cells with clear cytoplasm; in others there were large areas composed of acini containing colloid; and a few contained cystic structures of varying size. Frequently one tumor presented several of these types of tissue. In still others there was merely a marked increase in normal parathyroid tissue. While these last apparently constituted a simple hyperplasia of the glands, the consensus of opinion in the majority of other cases described was that they were true adenomata. There has been little or no uniformity in the coincidence of these tumors with various diseases, and no theory of etiologic relationship can be postulated on the meager evidence at hand. Several of the tumors have occurred in the absence of any other disease entity, or in acute illnesses with no possible connection. Others have been associated with chronic nephritis, osteomalacia, paralysis agitans, rickets, tetany, and epilepsy, but none in sufficient numbers to warrant definite conclusions.

In the series of 10,000 autopsies five cases of parathyroid tumor were found, each involving a single gland, the others being normal. These adenoma-like nodules presented the usual variegated structure with solid areas of clear or acidophile cells, thick cellular branching cords, areas of acini filled with colloid, and in two cases small cysts containing coagulated fluid. None of the tumors showed any invasive tendency. It is interesting to note that of these five cases four were associated with well marked chronic diffuse nephritis, the remaining tumor occurring in a case of acute yellow atrophy of the

liver with extensive degeneration of the renal epithelium. Of the four cases of chronic nephritis one presented in addition a carcinoma of the stomach. Also of considerable interest is a sixth case, again showing chronic nephritis, associated this time with an extreme pyloric stenosis, tetany, and calcium deposits in the mucosa of the ileum. In this instance five enlarged parathyroids were found, the largest measuring 9 by 5 by 4 mm., and all showing many eosinophile cells and numerous mitoses. This was considered to represent a simple hyperplasia of the parathyroid tissue, and no structures resembling adenomata were found.

More than a score of adenomata of the islands of Langerhans have been reported and it is probable that they are considerably more common than this number would indicate. The most recent description is by Warren (10), who gives a brief résumé of previous cases and adds four of his own. He makes a somewhat arbitrary distinction between mere hypertophy of the islands and true adenomata, stating that the latter must be at least 1 mm. in diameter, with a morphology and arrangement of cells similar to those of normal islands, and showing a definite fibrous capsule with evidence of compression of the surrounding pancreatic tissue. Most of the tumors described have been purely accidental findings at autopsy and have shown no constant etiologic relationships, nor have they produced any recognized functional change in carbohydrate metabolism. Three cases have occurred in diabetics, but of these two were of doubtful adenomatous nature. It must be borne in mind that so-called adenomata of any glandular organ may frequently be evidences of a regenerative or compensatory hyperplasia, although in the majority of the above cases no stimulus to such reaction is apparent.

In 10,000 autopsies only one adenoma of the islands of Langerhans was found.[2] It occurred in an otherwise normal pancreas and bore no obvious relation to the disease which caused death. In none of the cases of parathyroid or pancreatic tumors were any significant changes found in other endocrine organs.

[2] A recent autopsy not included in the series of 10,000 revealed a malignant tumor of the islands of Langerhans invading the stomach wall, and others of the same type have been described, notably that by Wilder, in which there were widespread metastases in the liver, and an extraordinary hyperinsulinemia, with corresponding hypoglycemia (12).

It is thus seen that tumors of the hypophysis and adenoma-like enlargements of the parathyroids and islands of Langerhans are by no means rare occurrences. The following case is of special interest in that it combines these lesions and presents additional changes in the ovaries, with enlargement of the adrenals. It offers anatomical evidence of the possible interrelationship of the various glands of internal secretion.

ABSTRACT OF CLINICAL HISTORY

C. R., a 22-year-old unmarried Spanish girl occupied as a laborer in a cigar factory, entered the Johns Hopkins Hospital in November, 1927, complaining of severe headaches and poor eyesight of about two years' duration. Her family history was irrelevant. Her past history was essentially negative save that menstruation did not begin until the age of 19. After this time, however, the menses were regular and apparently normal.

Two years previously, while at work, she had a sudden severe headache accompanied by nausea and vomiting. Following this, headaches were almost constant in the parietal and occipital regions. Believing them due to poor eyesight she consulted an oculist six months later and found that her left eye was practically blind and that vision was diminished in the right eye. Her eyesight became progressively worse. Occasionally she saw double and had mild attacks of dizziness. There were no further sensory disturbances and no motor paralyses. She had no convulsions or attacks of unconsciousness.

Examination revealed a well nourished young white girl, moderately obese and of small stature. There was very little axillary or body hair. The pubic hair was abundant but showed a tendency toward the male type of distribution. The mucous membranes were normal. Many of the teeth were soft and carious. The heart, lungs, and abdomen were apparently normal.

Neurologic examination elicited the following findings: The visual fields were markedly contracted and showed a definite bitemporal hemianopsia, with almost complete blindness of the left eye. The optic discs were pale but not choked, the pallor being more marked on the left. There was no nystagmus or strabismus. The remaining cranial nerves were normal. Both knee jerks were slightly exaggerated. The Romberg and Babinski tests were negative. The Gordon and Oppenheim reflexes were faintly positive on the left side, with a slight ataxia of the left leg in the heel-tibia test. The left hand also showed a slight ataxia. There was no apraxia, aphasia, or astereognosis.

The spinal fluid was entirely normal. The spinal fluid and blood Wassermanns were negative. The urine was normal.

X-rays of the skull showed a complete destruction of the sella turcica with evidence of beginning intracranial pressure.

In the absence of any clinical indications therefor, blood chemistry determinations were not carried out.

A diagnosis of hypophyseal tumor was made and a craniotomy was performed on November 9, 1927. It became immediately evident that the large bulging tumor mass filling the sella turcica and surrounding the middle cerebral artery and the optic nerves was inoperable and no attempt was made to remove it. Following the operation the intracranial pressure quickly rose and remained high despite several ventricular punctures. The urine was examined once shortly after the operation and showed a very slight trace of sugar. Nine days after the operation bilateral occipital trephines were made, without marked relief. The temperature remained high and the leucocyte count rose from 10,000 to 27,000. The temperature finally reached 107.3° and the patient died thirteen days after the operation.

Clinical diagnosis. Inoperable tumor of the hypophysis.

Anatomical findings. The autopsy was performed seventeen hours after death. Only the salient portions of the protocol are here recorded.

The body is that of a young adult white female, weighing 42 kgm. and measuring 157 cm. in length. It appears more like that of a child than of an adult. There is no edema. The skin is pale and smooth. There is very little axillary or body hair, save on the legs where it is quite abundant. The pubic hair suggests the male type of distribution. There is a moderate degree of obesity and the fatty panniculus over the abdomen measures nearly 3 cm. in thickness. The extremities are short but show no special abnormalities of the bony structure.

The face is round and the features present no striking characteristics. The breasts are small and undeveloped, with small nipples and unpigmented areolae. The external genitalia are like those of a child near the age of puberty.

The heart, lungs, spleen, liver, kidneys, stomach, and intestines are normal.

The pancreas measures 14 cm. in length and weighs 160 grams. It is firm in consistence. At the junction of the middle and outer thirds, lying just beneath the capsule, is a small firm nodule measuring 10 by 7 by 6 mm. It is encapsulated and sharply demarcated from the surrounding tissue. On section it is found to be composed of greyish white translucent tissue showing many dilated blood spaces. Further sections of the pancreas reveal no less than eight sharply outlined smaller nodules, from 3 to 6 mm. in diameter, resembling the first save that the blood spaces are not so prominent. They are scattered uniformly throughout the pancreas and show no special site of predilection. At least three are found within 3 cm. of the proximal end, and two are present in the distal third. The pancreas itself presents a normal lobulated structure and grossly shows no further changes.

The uterus is small and firm, measuring 6 cm. from cervix to fundus, and 4.5 cm. transversely. It appears normal. The tubes are normal. The ovaries seem enlarged, each measuring 3.5 by 3 by 2 cm. Both show a few small recent scars on their surfaces, and both have a peculiar soft, spongy consistence. On

section the stroma is quite pale and soft, as if made of loosely meshed tissue. Both ovaries contain numerous small cysts filled with a cloudy gelatinous material. These measure 4 to 7 mm. in diameter. A few small corpora lutea are seen.

The adrenals are large and firm, each weighing approximately 12 grams. A longitudinal section of one measures 4.5 by 1.2 cm. Grossly, their structure appears normal.

The thyroid is small and has a normal structure with small uniform acini filled with colloid. No nodules are seen.

Three parathyroids are found. Of these one near the left upper pole of the thyroid measures 3 mm. in diameter and appears normal. The others, found near the lower poles, are markedly enlarged, that on the left measuring 1.7 by 1.0 by 0.8 cm., that on the right 1.5 by 0.4 by 0.3 cm. They are solid in consistence, well encapsulated, entirely separate from the thyroid, and not infiltrated with fat. On section they are pinkish grey, the larger one showing a few small firmer slightly yellowish areas and a somewhat lobulated contour.

A small involuted thymus is present.

There is a large ragged operative defect in the left fronto-parietal region of the brain. The entire base of the brain from the medulla to a point well in front of the optic chiasm is covered with a great mass of soft, mushy, hemorrhagic, partially necrotic tumor tissue. This completely envelops the chiasm, the hypophysis, and many of the cranial nerves. It fills the sella turcica, which is large and irregular, measuring roughly 3 by 2 by 1.5 cm. The floor of the sella is thinned out and decalcified so that it can easily be cut with scissors. On section of the brain the tumor is found to extend up between the hemispheres, pushing the floor of the third ventricle ahead of it so that the ventricle is almost obliterated. The septum lucidum is spread open into a wide chamber which is filled with tumor. The tumor extends anteriorly so as to subtend the frontal lobes. The lateral ventricles are moderately dilated. The pineal body is normal.

The hypophysis is found embedded in the tumor mass within the sella turcica. It seems well encapsulated, but a thin sheath of tumor remains adherent to it. It is not obviously flattened and appears, if anything, slightly enlarged, the anterior lobe measuring 1.3 by 0.6 cm. on section. Grossly, its structure seems normal.

Microscopic findings. Serial sections were made of the greater portion of the hypophysis and several sections were taken from various parts of the adjacent tumor. The latter were unsatisfactory as the tumor was poorly preserved and partially disintegrated. The hypophysis is slightly enlarged but otherwise normal. The anterior lobe consists of acini separated by thin fibrous septa and made up for the most part of large polyhedral eosinophile cells with relatively small deep-staining round nuclei. By far the majority of the cells are deeply eosinophile and stain heavily in Bensley's Orange G-gentian violet granule stain. A few of the acini and a few scattered cells do not contain the acidophile granules. The nuclei of these cells are somewhat larger and do not stain so deeply as those

of the chromophile cells. There are numerous dilated blood spaces filled with blood. The pars intermedia shows a few small cystic spaces lined with a single layer of cuboidal epithelium and filled with a pink-staining coagulum. The posterior lobe is normal.

The capsule of the hypophysis is intact save at one point over the anterior lobe where the cells of the hypophysis come in direct contact with those of the surrounding tumor. The granule stain here shows a sharp line of demarcation between the deep-staining chromophile cells and the pale tumor cells. A small

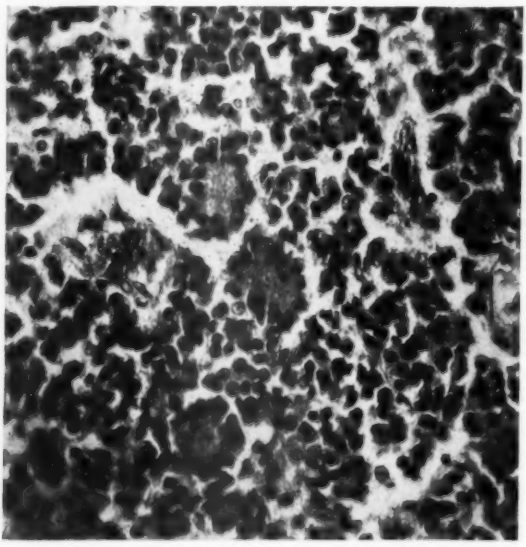

FIG. 1. TUMOR OF HYPOPHYSIS, SHOWING FORMATION OF ACINI—3 MM. OBJECTIVE

cluster of the former cells, however, extends out beyond the line of the capsule into the tumor and a few scattered cells both here and elsewhere in the tumor contain acidophile granules.

The best preserved portions of the tumor are made up of dense masses of cells of uniform size, or of cords one or two cells in breadth, and show a tendency to form acini (Fig. 1). The cells are large, polyhedral in shape but with indistinct outlines, and have round pale-staining vesicular nuclei, which are larger and less sharply outlined than those of the cells in the hypophysis. They frequently contain a nucleolus. The cytoplasm stains a faint bluish pink, and in the great majority of cells contains no granules. There are numerous thin-walled blood

spaces. The tumor thus resembles several examples of the chromophobe struma described by Cushing, or the so-called malignant hypophyseal adenoma described by other writers. The exact point of origin cannot be definitely determined.

The pineal body shows no changes.

The thyroid gland is normal.

The smallest of the three parathyroids is quite normal. The other two show striking changes, which are similar but most marked in the largest (Fig. 2). The

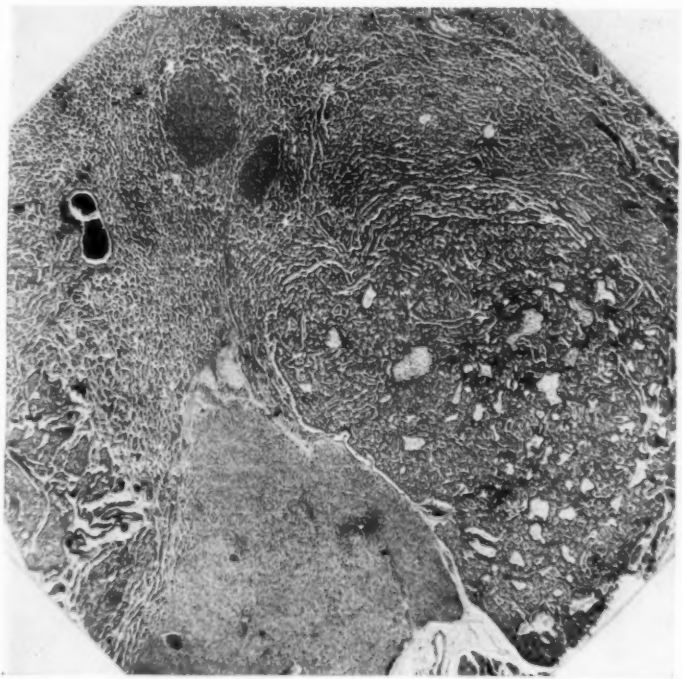

FIG. 2. TUMOR-LIKE ENLARGEMENT OF PARATHYROID—48 MM. OBJECTIVE

major part of the tissue is made up of bulky branching cellular cords, the nuclei being arranged in such a way that they form regular rows at the outer borders of the cell columns. The cells are round or cuboidal, with pale pink-staining cytoplasm, and sharply staining round nuclei (Fig. 3). The cell columns merge imperceptibly with large areas composed of uniform small acini containing colloid and made up of similar cells. In these areas a few scattered clumps of large eosinophile cells are seen. Still another type of tissue is found in several large, solid,

sharply circumscribed masses of cells showing no definite architectural arrangement, in which the cytoplasm is clear and the nuclei slightly more vesicular in character, with greater variation in size. No mitotic figures are seen. The solid masses are interspersed with fine fibrous septa and show numerous delicate capillaries. There are no cystic structures in either of the glands, and both are well encapsulated.

The thymus shows a fairly advanced stage of normal involution.

Fifteen sections were made of the pancreas at regular intervals from head to tail. These present a variety of changes, the most notable being the encapsulated

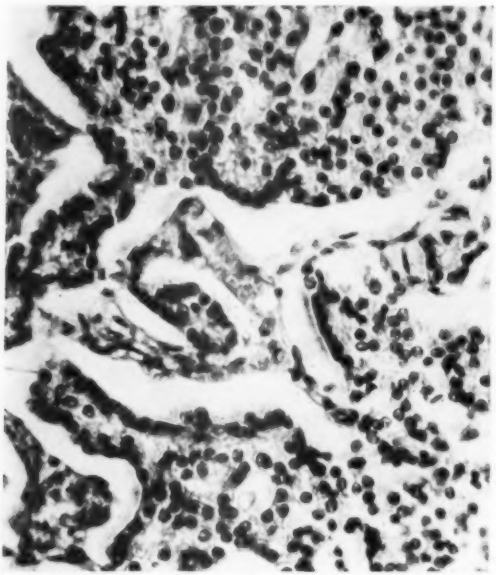

FIG. 3. TUMOR-LIKE ENLARGEMENT OF PARATHYROID—3 MM. OBJECTIVE

nodules described grossly. No less than ten of these are found, with few exceptions all practically identical in structure, though varying in size. All of the larger nodules have definite fibrous capsules and about many of them the pancreatic tissue shows evidence of compression. They are composed of delicate interlacing and communicating cords of cells which in every way resemble those of the islands of Langerhans (Fig. 4). The strands are from one to three cells thick and are made up of roughly cuboidal or cylindrical cells, vaguely outlined, having pink-staining cytoplasm and sharply staining round vesicular nuclei with finely granu-

lar chromatin. A few scattered cells contain cytoplasmic granules similar to those seen in the normal island cells, as shown by Bensley's neutral gentian stain. The cells are somewhat larger than those seen in the parathyroid and the nuclei are arranged centrally in the cell strands, with the cytoplasm toward the outer edge. The strands are separated by wide spaces in which run capillaries and delicate fibrous septa (Fig. 5). In two of the nodules several small branching duct-like structures are seen, lined with a single regular layer of tall columnar cells,

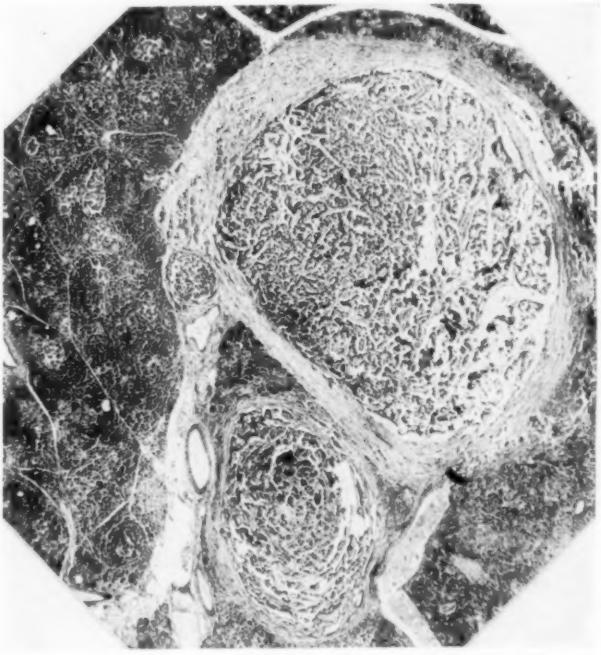

FIG. 4. ADENOMA-LIKE NODULES OF ISLANDS OF LANGERHANS—48 MM. OBJECTIVE

and closely resembling normal pancreatic ducts. They have no demonstrable connection with the tumor cells and no transitional forms or acinar structures are to be found in the nodules. One of these ducts traced by serial sections is found to pass through the capsule of the tumor nodule and make its way into the normal pancreatic tissue. The adenoma-like nodule of island cells has apparently proliferated about the branches of the duct, which itself is not a part of the growth.

The largest nodule contains large dilated blood spaces which make it appear almost angiomatous in character. In places the blood seems to come in direct

contact with the cell cords, but usually a thin layer of endothelium may be seen separating them. Another nodule is almost obliterated by dense hyalin fibrous tissue, a few small clumps of island cells being left in the center. A third nodule is freshly necrotic and its architecture destroyed, probably owing to some interference with the blood supply. The surrounding tissue is infiltrated with a few leucocytes.

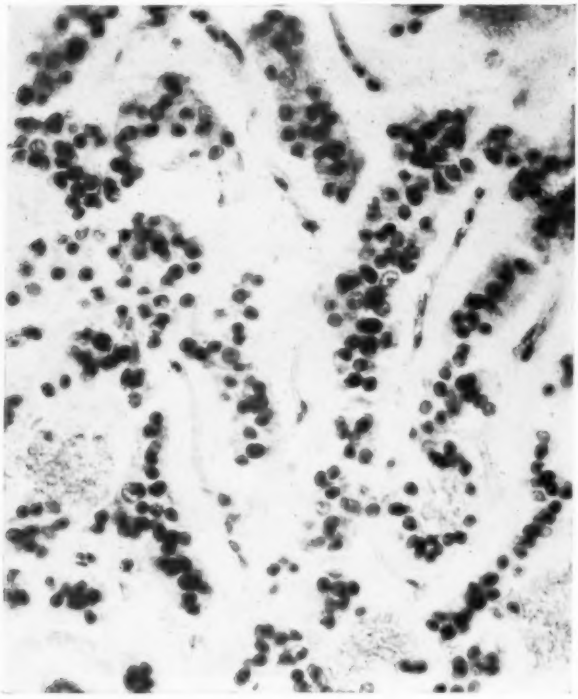

FIG. 5. ADENOMA-LIKE NODULE OF ISLANDS OF LANGERHANS—3 MM. OBJECTIVE

The acinar portion of the pancreas is for the most part normal. Scattered here and there are occasional localized areas in which the acini are dilated, their cells thin and pale-staining. This is presumably the result of obstruction of the corresponding terminal branch of the duct, due perhaps to pressure by one of the nodules. Some of these areas show a slight increase in fibrous tissue and are sparsely infiltrated with polymorphonuclear leucocytes,—undoubtedly a terminal

inflammation. The pancreatic tissue contains many normal islands of Langerhans, a goodly number of which are unusually large.

The adrenals are moderately enlarged and contain abundant lipoid material, but show no special alterations.

The ovaries contain numerous small cysts lined with several layers of round or cuboidal cells and filled with a pink-staining coagulum. These resemble typical Graafian-follicle cysts. Immediately surrounding them is a loose layer of large vacuolated cells which are found to contain fat in small droplets. Elsewhere the stroma is loose and edematous, its meshes being separated in places by fluid. The stroma cells are swollen and vacuolated, but do not contain fat. Occasional corpora lutea are seen, made up of large fat-holding cells. There are surprisingly few ova, but those that are found appear normal.

The uterus is normal.

The significance of these various changes in the endocrine system is obscure. That there is an intimate functional correlation of the glands of internal secretion has been established beyond any reasonable doubt. The nature of such correlation and of the stimuli which bring about various related changes in the members of the system is still a matter of conjecture. It is well known that the hypophysis is closely related to the reproductive organs, to the pancreas, and perhaps less evidently to the adrenals and thyroid. Its relation to the parathyroids is less clear, but there is at least some evidence that in acromegaly the parathyroids become enlarged.

In the present case definite anatomical changes are found in the hypophysis, parathyroids, and pancreas. It seems more than probable that they are related, but the evidence is insufficient to draw such a conclusion definitely. In the absence of detailed clinical data and blood calcium and sugar determinations it is impossible to ascertain whether or not the tumor-like parathyroid or island tissue had any functional activity. The presence of a small trace of sugar in the urine immediately following the brain operation indicates at least that there was no marked hyperinsulinemia. It is possible that the hypophyseal tumor by antagonistic action produced some stimulus to compensatory hyperplasia in the parathyroids and islands of Langerhans, with resultant formation of adenoma-like nodules. It is also possible that the various tumor-like phenomena were purely unrelated coincidences. The case is important, however, in the light of its unique anatomical findings, which may find confirmation or a satisfactory explanation in some future investigations or discoveries.

SUMMARY

A case is reported in which there was a large adenoma of hypophyseal tissue associated with adenoma-like enlargements of the parathyroid glands and the islands of Langerhans, and with moderate enlargement of the adrenals and ovaries.

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JOHN HUNTER, HIS ENEMIES AND HIS FRIENDS[1]

MANFRED S. GUTTMACHER

In talking about John Hunter I feel that one should not attempt to reproduce his life's calendar or render a catalogue of his virtues and accomplishments. His spirit can never be caught in so orderly a portrayal. Despite the fact that he mounted and described with his own hands more than thirteen thousand museum specimens, he was never a stolid drudge and never an uninteresting man. He was a fascinating, vivid and daring fellow dominated greatly by moods and guided by prejudices.

When I was in London, Mr. Plarr, the very charming and delightful librarian of the Royal College of Surgeons, generously sympathizing with my enthusiasm for the great patron saint of the College, put at my disposal the original Hunter manuscripts and the other remarkable Hunteriana of the College. One day Mr. Plarr pointed out to me in the greatest Reynolds portrait of Hunter (there are three) the barest shadows of legs to either side of the head. The story of their presence there is well known. Hunter had been urged by his friends to have his portrait painted. At that time he had neither the inclination, the money, nor the leisure to give in to this whim of theirs. Finally, Sharpe, an engraver whom Hunter had previously befriended, pled with him,—protesting that he would make a great engraving of the painting and thereby win for himself fame and a living. Hunter finally yielded. He very naturally went to Reynolds, his famous neighbor in Leicester Square, and the good friend of his late brother William. Reynolds found him, with his restless impatience, a very poor subject. One day, while sitting for Reynolds, he left off his nervous squirming and fell into a revery. Who knows what that brain was conjuring over? Perhaps it was that dream of his of making man capable of living a thousand years by freezing him, storing him on ice, and then thawing him out centuries later to live out his allotted

[1] A paper presented before the Johns Hopkins Historical Club at the John Hunter meeting, February 18, 1929.

span. Reynolds grabbed the moment, swiftly turned the canvas about, and sketched the head of that great masterpiece between the legs of his former delineation. This, it seems to me, must be the plan of a brief presentation of Hunter's life. Even though he was eminently human one cannot treat him like an ordinary man, one must grasp isolated moments to get him as he was. A common fault of his biographers is that they lay too little stress upon the period

FIG. 1. READ ENGRAVING OF JOHN HUNTER, MADE WHEN HE WAS A VERY YOUNG MAN

This, as well as the other illustrations, is in the possession of the author

in which he lived. This is probably in large measure due to the fact that they have followed Ottley's life of Hunter. Ottley was almost a contemporary and he naturally felt it unnecessary to reproduce the eighteenth century for a group of readers who themselves had lived in it.

A rebel in science and an ardent Tory in politics Hunter played a vital part in many phases of London life and they in turn profoundly

affected him. Eighteenth century London is fascinating and an insight into it is vital to any real understanding of Hunter. It is a

FIG. 2. ENGRAVING OF WILLIAM HUNTER, TAKEN FROM A DIPLOMA THAT HE ISSUED TO STUDENTS IN HIS SCHOOL OF ANATOMY

rather easy period for us of the twentieth century to live ourselves into, for in most respects it is more like our century than was the intermediary one.

About John Hunter's relationship to his brother William, little need be said. Despite the fact that they both had the same major pursuit in life they were totally different. William was rather tall, with fine features, and exquisite hands. John, according to the note that I saw in Clift's own hand, was but five feet two; he was stocky, almost bull-necked, reddish haired, with blunt features. Each had the temperament that one would expect with such a physical make-up. William moved with measured steps. He was a great drawing-room favorite, a charming, suave patron of the arts, and, with it all, one of the century's keenest anatomists. He was the first man to deliver an English Queen. It was to him that Dr. Johnson wrote asking him to present his *Journey to the Hebrides* to the King. He amassed during his life one of the greatest private collections of paintings and rare books in all England. John was blunt, blustering and amazingly undiplomatic. He swore so much that the publisher of his surgical lectures apologizes for taking the liberty of omitting the lecturer's frequent oaths,—protesting they could add little to their substance and might produce great offense. Fortunately, there are preserved to us a few such characteristic snatches as his description of a bullet "having gone into the man's belly and hit his guts such a damned thump that they mortified," and the reply to an Englishman who wished permission for a French friend to visit the museum, "If your friend is in London in October (and not a damned Democrate) he is welcome to see it, but I would rather see it ablaze, like the Bastille, than show it to a Democrate, let his country be what it may."

While John was a stubborn man, with an uncontrollable temper, William seldom lost his. He was very jealous of his claims to scientific fame. It must have greatly irked him to have his pupil and younger brother elected ahead of him to the Royal Society. When their great quarrel began it is not easy to ascertain. Peachy suggests 1777 or 1778. However, we find in a postscript in one of Tobias Smollett's letters to William in 1763, "I cannot help expressing the eager desire that your brother's future conduct may entitle him to a revival of those favorable sentiments in you which he has indiscreetly forfeited." But surely their final rupture did not come until many years later. There is nothing to suggest that their reconciliation occurred at William's deathbed, as some biographers would have us believe. At

this time there appears in the press a public appeal to former pupils for funds with which to bury their great teacher,—

April 4, 1783: "The writer of last Wednesday recommends that every gentleman of the Faculty in London who studied under the celebrated Dr. Hunter deposit one guinea at a certain banker's in order that his remains should be interred with every possible mark of respect. It is well known to the immortal honor of this great man that all his fortune was locked up in his grand museum and therefore, it is impossible for the executors to show that respect which is so justly due to the most celebrated anatomist of the present age. . . . . A Chatham was a great character, a Garrick deserved fame, and a Hunter was in his professional line equally as great."

Certainly, John did not offer to bury his brother. In the list of those attending William's funeral, which I found in a London contemporary paper, John is not included.

On Saturday, at eight o'clock in the evening, the remains of William Hunter, M.D., were interred in the vault under St. James' Church. They were attended by his nephew, Mr. Bailey (as chief mourner), Dr. Pitcairn, Sir George Barker, Dr. Fordyce, Dr. Heberden, Mr. Cruickshank, Mr. Combe, Mr. Birmie (his draughtsman), and a few other friends.

We do know that after William's death, in his lectures to his students John always paid great homage to his brother's character and his great ability as an anatomist. Knowing the personalities of the two it seems to me more than likely that John would gladly have become reconciled to his brother but that the latter was probably adamant.

John Hunter was married to Anne Home, the daughter of an army surgeon, in 1771, two months after the publication of his first work, "A Treatise on the Natural History of the Human Teeth." All the circumstances that we know of their marriage seems so typical of John Hunter! They had been engaged for many years—suddenly, on the meagre proceeds of his first publication he decided that they get married. It was not like him to procrastinate when he made up his mind to anything. He waived the usual amenities of publicly declaring his intentions days in advance, but dashed off this note to his brother William:

Dear Brother,

Tomorrow morning at eight o'clock, in St. James's Church I enter into the holy state of matrimony. As that is a ceremony which you are not particularly

fond of, I will not make a point of having your company there. I propose going out of Town for a few days; when I come to Town I shall call upon you. Married or not married, ever yours.

JOHN HUNTER.

Then he got his license and within twenty-four hours he was married.

The Natural History of the Human Teeth is the only one of his books published by a bookseller. It was very common in Hunter's time to have copies of the authors' manuscripts pirated away by the booksellers to Dublin, where an illegitimate edition of the new book was hastily got out and sold in London without having to pay the author's royalties. John Hunter met this in his usual direct manner. He had a press erected in his home and there he printed and sold his own works. In this book Hunter publicly acknowledges his relations with the dentist, Spence. One of the charges reiterated against Hunter in later years was that when he started practice in London he began under the auspices of "Old Spence and Sons," who were barbers and dentists. Unquestionably the accusation was true. Hunter did make his first shillings in their office. This whole relationship shows Hunter in a characteristic light. Rather than starve during those first years as surgeon he sought honest but lowly labor with fellow Scotchmen. He bothered little about their professional rating. While he was thus engaged in a manner that was considered beneath the efforts of his fellow surgeons, he collected material for a book on the teeth, which proved to be better than any previously written on that subject. It was also like him not to have tried to conceal his relationship with the Spences.

Hunter was as great a teacher as he was a scientist. Few men have had a galaxy of greater pupils than he. One of them, Gibson, is recorded as coming from Baltimore. Neither Cordell nor Kelly makes mention of him, and thus far I have been unable to find any information about him. By his fellow surgeons and teachers of medicine Hunter was looked upon as an impractical idealist, an innovator or a notoriety-seeker. The London of his day was either pro- or anti-Hunter. He allowed no neutrals. Men were his friends or foes. None claimed more frequent notice in the general press than he. He was the Samuel Johnson of medical London. I do not say this idly, either. In many ways they were alike. I find it most amusing

FIG. 3. SIR JOSEPH BANKS, PRESIDENT OF THE ROYAL SOCIETY
The Wagstaff engraving of the Phillips portrait

to conjure up before my mind those two giants face to face—they would surely have been attracted to each other—even though each knew relatively little of the other's field. Certainly no group could have long held two such lions and had peace in its midst. I have

looked in vain for evidence of intercourse between them. They must have known each other—they had such good mutual friends as William Hunter, Dr. George Fordyce, Edmund Burke, Sir Joshua Reynolds and Sir Joseph Banks. Sir Joseph Banks himself forms a very interesting study. He was a fine man with a fine intellect. Few men better illustrate the close relationship between the arts and the sciences still existent in England in the eighteenth century. It was to his charming home in Soho Square, which happily is to-day one of the best examples of Adams houses existing in London, that Josiah Wedgwood brought his first successful copy of the Portland Vase to exhibit it to the cognoscenti. Samuel Johnson actively electioneered to have Sir Joseph elected to his famous Literary Club. The quarrel between the Hunter brothers greatly grieved Sir Joseph and he made many fruitless efforts to bring them together again. It is interesting that John Hunter, Sir George Baker, and Everard Home attended Sir Joshua Reynolds in his last illness. Hunter performed the autopsy in which they found a cirrhotic type of liver weighing 11 pounds.

Any surgeon, who would entertain at his own dinner table the first Esquimaux to reach London, who would drive a herd of bisons through the streets, who could almost daily be seen at Earl's Court wrestling with a little bull presented to him by the Queen, or leading about a couple of leopards, would be looked upon with suspicion by the conservative medical leaders of any day. I fear then, as well as now, many of them were "men of measured merriment." Their sense of propriety must often have been sorely violated by John Hunter. By the youths of the day he was rightfully looked upon as the man who was pointing the way to the surgery of the future—those most eager to learn followed him. When a whale was washed ashore at the mouth of the Thames he took them with him and like the Swiss Family Robinson they climbed on top of it and dissected it. When an elephant died in the Royal Menagerie at Kensington he and his thirty pupils, at the request of George III, went out to dissect it. When a mummy was brought from Egypt it was Hunter who was called to examine it. This was indeed queer business for a class in surgery.

One of the students wrote: "In his lectures on surgery he entered but little into the minuter details of practice. He gave little or no account of the operations of surgery but confined himself almost

exclusively to the theory and principles of the art." And this great surgeon preceded the pedagogic innovator Halsted by more than a century. To Astley Cooper, who asked whether he had not enun-

FIG. 4. EDMUND JENNER
From an illustration in the European Magazine in 1804

ciated a different view of the subject in the course of lectures in the preceding year, he replied: "Very likely I did. I hope I grow wiser every year." To Coleman he once said: "Never ask me what I have said or what I have written, but if you will ask me what my present

opinion is I will tell you." After giving his views on a subject in a lecture he suddenly stopped, saying, "You had better not write down that observation, for very likely I shall feel differently next year." I feel, as Stephen Paget has pointed out, that nothing gives a clearer

FIG. 5. ERASMUS DARWIN
The Cooper Engraving of the Ranlinson portrait

insight into the character of Hunter than a letter that he wrote, between excruciating attacks of angina pectoris shortly before he died, to an acquaintance in Africa who had sent him, as a gift, two birds. In this reply he asks for all species of swallows and for ostrich eggs. Then he goes on, "If a Foal camell was put into a tub of spirits

and sent I should be glad. Is it possible to get a young tame lion, or indeed any other beast or Bird? If camelions were sent it should be in the spring as then we could feed them Flys during the summer. Are there any cuckews with you? I want everything respecting the Bee tribe, such as wasps with their nests, also hornets with theirs. They are a very large tribe." He was then sixty-five years old. Can there be any wonder that such a man, despite his very nervous and hesitant delivery, his obscure and complex style, should have been the most successful teacher of his day?

I sometimes wonder how much the cause of evolution owes to John Hunter. Certainly vaccination owes much to him. In that perfectly delightful series of letters between Hunter and his devoted pupil, Jenner, one can readily see the goading source of Jenner's stimulus to scientific inquiry. Erasmus Darwin—himself a fascinating man, with many of the Hunterian characteristics, and the devoted friend of the first of the Wedgwoods—was one of Hunter's pupils. In many of the passages of his curious scientific poems, hints at evolution may be found. Charles Darwin, in his short autobiography, acknowledges his grandfather as his great scientific heritage. When one sees in the museum of the Royal College of Surgeons well ordered phylogenetic series of specimens arranged by Hunter, one wonders whether the germ of evolution was not planted there. A 1782 number of *The Gentleman's Magazine* says, 'Mr. Hunter facetiously observed that in placing the negro above the monkey great honor was due to him, for although a man, he could hardly be called a brother. He also remarked that our first parents, Adam and Eve, were indisputably black." After all it was at about this period that the eccentric fellow Scotsman, Lord Monboddo, was being ridiculed for his doctrine that man had a tail and was descended from the ape.

Hunter was very conscious of his great difficulty in expressing himself clearly. In speaking of his treatise on venereal disease he told Joseph Adams, "In order to render the language intelligible, I met a committee of three gentlemen to whose correction every page is submitted." Sir Gilbert Blane, Dr. George Fordyce, and Dr. David Pitcairn were the members of this editing board. The cause of this great difficulty in expressing himself has been analyzed by many. His foes either attribute it to unfamiliarity with good books or a

purposeful effort to cloak ignorance. Although not a great reader, Hunter undoubtedly read more than is commonly believed. A catalogue in the British Museum, got out by Christie for their auction on February 1, 1794, is headed "Well Chosen, Select Library of Scarce Books—The Property of John Hunter, Esquire, Deceased." It contains a large number of volumes of all types, many of them in French and in Spanish, languages that Hunter probably learned to read on the Belle Isle expedition. There are about ten books printed before 1600 and one incunabulum. Some of the books were undoubtedly gifts and perhaps Mrs. Hunter, who was very much interested in the arts and literature, included some of her own. In a letter that Tobias Smollett wrote to John Hunter from Italy in 1763, he says, "You say that you should be glad to have every curious book on the face of the earth, but I should be afraid of sending you some that you have already." This surely suggests an interest in books.

Unquestionably, Hunter got little from his short stay at Oxford. He went there fresh from his own independent investigative labors in the dissecting room, while recuperating from a probable tuberculous infection. Certainly not very auspicious circumstances under which to attend that University! The second claim of his antagonists that he tried to throw obscurity over his ignorance is not worthy of discussion—his whole personality and his discomfiture at these difficulties speak against it. Buckle, who in his history of *Civilization in England* ranks Hunter with Aristotle, Harvey, and Bichat, says, "It sometimes seemed as if the understanding was troubled by the grandeur of its own conceptions and doubted what path it ought to take." He strenuously objects to the theory that the lack of education was responsible for his complex and unintelligible style, citing examples of men who were uneducated and who wrote clear and facile prose. Undoubtedly Hunter's own self-consciousness was a big factor. When Hunter let himself go, as he often did in his letters, he wrote delightfully. Another factor was that in his desire to be intellectually honest he inserted so many qualifying clauses that one easily loses the main argument. What could be more delightful than the reply to Jenner when he invited Hunter to be godfather for his first-born?

Dear Jenner,—I wish you joy; it never rains but it pours. Sooner than the brat should not be a Christian I will stand godfather, for I should be unhappy if the

poor little thing should go to the devil because I would not stand godfather. I hope Mrs. Jenner is well, and that you begin to look grave now you are a father.

Yours sincerely,

J. HUNTER.

I should like to speak of Hunter's relationship to his professional hater, Jesse Foot, and his friendship with that curious quack, Van Butchell. But first, it would be well for us to glance at the setting in which they occur. The London of Hunter's day was hardly a twentieth of its present size. The first intellectual circle of the period was surprisingly small, even though it was heterogeneous, for it was before the day of intense specialization, and artists and scientists mingled together. All of its members would become aroused over personal issues in a way that to-day is unknown. There was in the eighteenth century a lack of scientific sophistication that is very amusing. Even Sir Joseph Banks, President of the Royal Society, was at a loss for an idea to explain how black negroes could have coffee-colored children. It was an age in which new wonders were fast developing. Electricity was beginning to come into its own and everything was viewed with credulity. There was a fine personal and intellectual toleration, however.

It was only two years before Hunter's birth that Mary Tofts gave birth to her rabbits in the little village of Godalming. About the time of Hunter's birth the bone-setter, Crazy Sally Mapps of Epsom, an enormous fat, ugly, drunken woman, was made famous by being consulted by Sir Hans Sloan, a President of the Royal Society, in the case of his niece. In this case she successfully reduced, at the Grecian Coffee House, a dislocated shoulder of nine years' standing. It was a little later that Johanna Stephens successfully mulcted five thousand pounds from the people and the Parliament of England for revealing the formula of her famous powder to dissolve stones. Among the group who endorsed her in a written testimonial were the Archbishop of Canterbury, Lord Baltimore, Godolphin, and the medical men, Samuel Sharp, Caesar Hawkins, and William Cheselden, Hunter's favorite teacher. The powder consisted of egg shells and snails, both calcined. A decoction was made by boiling these with some herbs, together with a ball which consisted of soap, swine's cresses and honey and water. To this was added wild carrot seeds burdock seeds,

ashen keys, and hips and haws. These were all then burned to a blackness. Toward the middle of the century, Chevalier Taylor, "Ophthalmiater, Imperial, Pontifical, and Royal," was taking England by storm. Then came Dr. Katterfelto, spurious F.R.S., of the Death

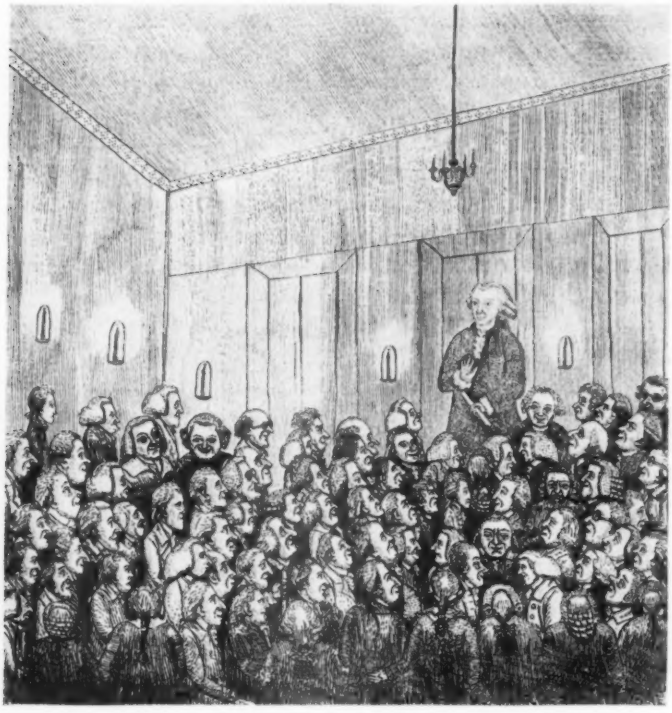

FIG. 6. KAY'S ENGRAVING OF JAMES GRAHAM LECTURING TO THE YOUNG BLOODS OF EDINBURGH ON GENERATION

Hussars of Prussia, who demonstrated, under a microscope, for a few pence, the terrible animalcules that were responsible for the outbreak of influenza. Even the Prince of Wales squinted and applauded. James Graham, the most fascinating quack of the entire group, an Edinburgh man, and an able and original thinker,

made in 1783 more than thirty thousand pounds by his lectures on generation and by the rental of his Royal Patagonian Bed. This remarkable contrivance had electrical sparks jumping all about it. Its use during conception guaranteed that "Sons springing from the bed like Mars shall prove and daughters beauteous as the Queen of Love." Lord Gordon and many other noblemen paid a hundred guineas for its use. After leaving Edinburgh Graham practiced in Baltimore and other parts of America, returned to England, founded a society in London to treat deafness, and dissolved it as soon as he had the dues of enough life members, invented his bed, championed earth bathing, fresh air, long fasts, alcoholic prohibition, and finally died a Methodist minister in Scotland.

In the *Morning Post* of September 29, 1776, we find the following medical advertisement. It is a very fair specimen of the myriad that daily appeared.

> Mr. Lattes, a Piedmontese gentleman, begs leave to acquaint the nobility and gentry that by a long course of experiments he has discovered the wonderful secret of procreating either sex at the joint options of parents. Should their desire be to have a daughter, the success cannot be warranted with absolute certainty, though the chance will be highly in favor of such an event, but should they concur in their wishes to have a son they may rely that by strictly conforming to a few easy and natural directions, they will positively have a boy. This may seem a bold and rash assertion but it has not failed in a single instance during 16 years. Mr. Lattes can have no view of imposing on the public, since he expects no endowment or gratuity till the completion of what he warrants. Should Mr. Lattes meet with encouragement on this occasion it will prompt him to offer to the public a most safe and easy method toward curing barrenness to succeed in almost twenty instances out of a hundred, a discovery which naturally occurred in the course of his main investigation.

For their physicians the common people still greatly favored the unborn (caesarian delivered) seventh sons of seventh sons. Persons who themselves had hernias and whose fathers before them had had hernias were considered preëminently fitted to treat the same malady. The deaf and dumb were employed to draw, intuitively, from a large collection of liquids and salves, the one needed.

One gets perhaps as accurate a picture of a people from their amusements as from any source. During Hunter's lifetime animal baiting was still one of the chief sports. Anatomical monstrosities of all types

were shown on the chief streets of London for gain,—dwarfs with monstrous craws (undoubtedly Cretins); Mrs. French, the lady with horns growing from her head; Mary Gasson of Rye, who was pregnant for six years without going into labor; the Everett baby, of astonishing size; Mr. Wright, who weighed over 500 pounds; an albino and his sister "whose eyes are in constant motion," (I believe the first description of nystagmus in albinism); the sapient pig; live fairies; and mermaids; all these drew large crowds. Live cat-eating contests were not infrequently reported in the London papers.

The World, June 9, 1790.

A man for a trifling wager actually ate a live cat, at a public house in Windsor on Tuesday evening last—a bystander thus related the process of this essay of brutality.

The man secured the fore and hinder legs of the animal in his hands and his first attempt was to seize the animal on the back part of the neck, which he effected, but not sufficiently so as to deprive the cat of the power of resistance, for puss caught hold of his face with her claws and produced a copious stream of blood. The man monster, in his turn, made a formidable attack on the head of his antagonist and by repeated bites soon deprived it of existence. He then with great coolness devoured his prey, not even using the ceremony of stripping off the skin; and in the space of an hour nothing but the bones was left as the memorial of a most astonishing instance of the exercise of a brutal appetite, and the degradation of a human nature. It is computed the cat weighed nine pounds. The more distinctive minutia of his transaction was too bad to be related.

Then there is the tragic record of the Hottentot Venus who was shown by a Jew for gain. Many letters of complaint were sent to the press protesting against alleged cruelty on the part of the manager. He met the storm by having his subject baptized a Christian. All felt satisfied. It was evident that they had been wrong. Any man who is enough interested in Venus' soul to have her baptized must be a kindly master. It was fortunate for her that he did so, for a few months later she died in Paris. Giants had a great vogue in eighteenth century London, particularly Charles Byrne, who was Hunter's famous giant. It is interesting that Graham publicly invited him to be the first to use the Royal Patagonian Bed, but Byrne refused. This newspaper account gives interesting clinical testimony that he was then already in the late stage of acromegaly.

Parker's General Advertiser—1782.

We are credibly informed that Dr. Graham of Pall Mall has visited the giant and has given him a very pressing invitation to h's promenade. The doctor has also made him the first offer of the Patagonian Celestial Bed, but this honor the giant, with the utmost delicacy, modesty and politeness, declined accepting for very particular reasons.

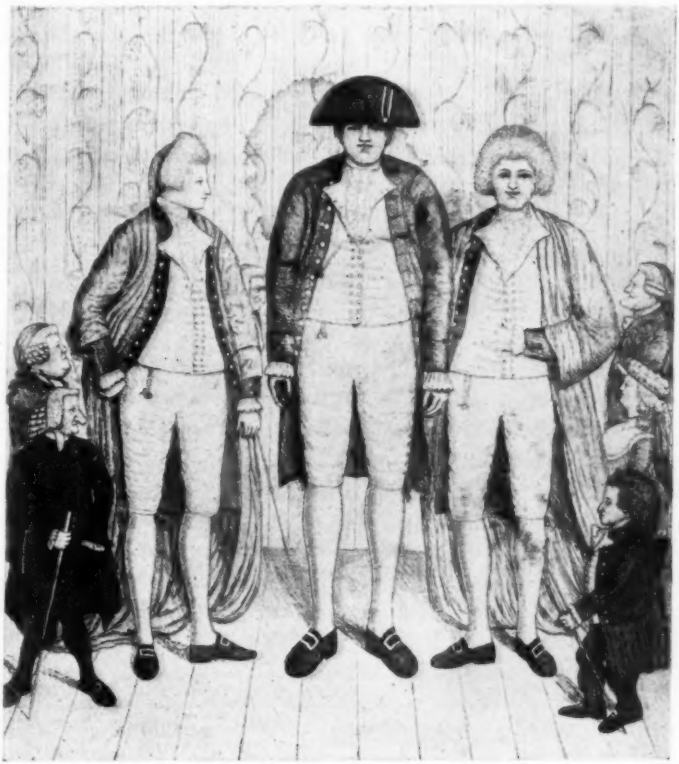

FIG. 7. KAY'S ENGRAVING OF CHARLES BYRNE, HUNTER'S GIANT, FLANKED BY THE KNIPE TWINS

The figure in the left foreground is Andrew Bell, the first Editor of the *Encyclopedia Britannica*. The profile in the rear is that of Lord Monboddo. The dwarf is Georgia Cranston, well known in Edinburgh for his small stature and the large size of his alcoholic draughts.

The giant is said to be a perfect stranger to the rites and mysteries of the Goddess Venus. He is about 23 years of age, is a sensible man and behaves with great propriety and docility when properly treated.

Other accounts attest to the poor wretch's bad disposition. No wonder that a man nearly blind and dying of a brain tumor was a bit truculent while being exhibited to the gaping rabble.

John Kay, the remarkable caricaturist of Edinburgh, who had his barber shop just across from the buildings of the Scotch Parliament, made more than four hundred engravings of famous characters of his day. The one of this giant, Charles Byrne, with the Knipe twins, is so little known that I was able to contribute a copy of it as a new Hunterianum to the Royal College of Surgeons in London.

Jesse Foot, the malignant professional enemy of John Hunter, began his published campaign against Hunter in 1786, with *Observations Upon the New Opinions of John Hunter in His Late Treatise on the Venereal Diseases*. A word about Foot. He was born in England in 1744, was a house surgeon at Middlesex in 1766–1767, and then went to practice in the West Indies and later in St. Petersburg, Russia. He then returned to London, where he opened an office on Dean Street, Soho. The cause of his intense animadversion of Hunter has long been a matter of conjecture. Farington, in his contemporary diary, says, "Foot, the surgeon, became rancorous against John Hunter because the latter had seemed to describe as not necessary a bougie which Foot had invented." Ottley and most others feel that Foot wanted to create two factions in London, one of Hunter's friends and the other of his enemies,—of which he would be leader, thereby gaining for himself a position of preëminence to which he could not otherwise aspire. He probably realized very well that he could fan the flame of hatred that was still burning in the heart of many Englishmen against the successful Scotch immigrants. When Bute had risen to power as Privy Councillor actual anti-Scotch riots had occurred in England. David Hume, the Scotch historian and philosopher, had said, a few years before, "The English rage against the Scotch is daily increasing."

Two years after his criticism of the treatise on Venereal Disease, he published an eighty-six page pamphlet, *An Essay on the Bite of a Mad Dog, with John Hunter's Treatment of the Case of Master R, and Also a Recital of the Successful Treatment of Two Cases by*

Jesse Foot, Surgeon. The opening motto was taken from Voltaire, "Rien n'est beau que le vrai." This he dedicated to Percival Pott, a man with whom John Hunter had openly quarreled because Pott had refused to grant him recognition for having demonstrated to him in the Hunter dissecting room the condition of congenital hernia. By this time the quarrel between Foot and Hunter had become a public matter. He says, "Considering the Terms upon which Mr. John Hunter and I stand, it becomes me to be more fully explicit." He then quotes Hunter's letter to the boy's family physician, "I saw him only a few hours after the bite and I immediately applied the caustic. I rubbed in mercury so that the mouth became sore. Twice I applied a caustic to the whole—but I am inclinable to believe I did not touch every part where the teeth had been—from the termination of the case." Let me assure you that this type of intellectual honesty was as rare in the eighteenth century as it is in the twentieth. Foot met this magnificent admission scornfully, "A modest man, a man of feeling, or a good surgeon would have blushed at such an apology." Foot then reviews literature dealing with the excision of bites, particularly an experimental paper on snake bites, sneeringly adding, "If he had ever deigned to read he would have found that by Fontanna's experiments excision in snake bites never fails while caustic never succeeds." He mentions an interesting case reported by Dr. Nourse in the Philosophical Transactions, 1737–8, in which nineteen months intervened between the bite and the onset of the hydrophobia.

Foot's third publication was a scandalous *Life of John Hunter*, published in 1794, shortly after his death. It is claimed that Foot got four hundred pounds from Hunter's foes for doing this job. In his introduction he says, "I write more to inform than to praise." He begins the life thus, "I shall suppose that when John Hunter was in the arms of his nurse, he was seen exactly like any other child in a similar situation . . . . that he was neither detected playing with a serpent, thrusting his hands into the mouth of a lion, nor staring the keen eyes of the eagle through and through, 'till he forced him to blink at his own, the keenest." He reiterates the frequent claim that Hunter's works were written by another, meaning, of course, his friend and fellow Scotch physician, Tobias Smollett. This accusation was

given birth when Smollett let the Hunters use his publication, *The Critical Review*, as the vehicle for their polemics against the Monros. Foot says that Hunter selected obscure subjects for his papers because "he aimed to be admired, rather than useful, marvelous rather than true, difficult rather than important." He decried his surgical training, saying that he reversed the usual scheme of things by taking much anatomy and little surgery. He neglects, of course, his extensive surgical experience while on the Belle Isle expedition. "His being totally unacquainted with materia medica rendered his prescriptions bold and informal." Many of us may see in this another way in which Hunter was pointing out the direction of the future.

The following year a fourth publication, *Dialogues Between a Pupil of the Late John Hunter and Jesse Foot*, appeared. It begins by declaring that Foot never had any personal animus against Hunter. In it he attacks Erasmus Darwin as well. The chief reason for this attack is the latter's willingness to accept his teacher's scientific statements as truths. Foot further states that Hunter himself did not believe what he wrote and he doubts that Hunter ever inoculated himself with the venereal virus as he reported. In 1808 he wrote a monograph contrasting the views of P. S. O. Mahon and those of John Hunter in regard to venereal disease. In 1812 he reviewed Everard Home's *Diseases of the Prostate Gland*, in which he denied Home's claim that there was a middle lobe and criticizes him for his haughty tone, declaring him a true member of the Hunter family. In addition, there were two anonymous publications that were almost certainly written by Foot, one in 1793, the other in 1794, dealing with Hunter's quarrel at St. George's, and the disposal of his museum after his death.

Much light has been thrown upon this calumny by two large folio volumes acquired for a meagre twenty-one pounds by the Burrows Welcome Museum three or four years ago. I had the good fortune to examine these volumes. They are the beautifully bound Hunter Scrap Books, arranged by Foot. The books appear to be unfinished and were probably being added to by Foot at the time of his death, in 1826. Apparently there was never any intention of their publication. The illustrations are of various kinds, many of them are repeated several times; a steel engraving of Peter Camper appears four times. There are Belle's engravings from Hunter's *Anatomy of*

the Teeth, the title page and engravings from Nuck's *Sialographia*, the title page to Vesalius, *De Fabrice*, etc. Then there are about a dozen crayon and water color sketches believed by Mr. Victor Plarr to have been the work of Beaumont, who was at that time the popular miniature painter of Edinburgh. One of these sketches represents Hunter being horsewhipped by Peter Camper. This no doubt refers to the dispute between Hunter and that very able Dutchman over the

FIG. 8. JESSE FOOT, ESQR.
The Freeman engraving of the Opie portrait

priority claims for the discovery that the bones of birds have air cavities. Another represents Hunter in conversation with his friend Van Butchell, the dentist. Opposite the reference to the strange cerebral attack which Hunter had, and which Home described as an "ecstasy," is a very salacious nude figure. The final sketch represents Hunter's body being carried home from St. George's with a lot of squawking magpies on top of the sedan chair.

These two volumes suggest very strongly the work of a paranoid

man. This was no plaything. The life blood of the editor went into it. Whatever it was that started Foot's hatred for John Hunter we don't know, but it certainly seems to have passed the bounds of normal hate. Freeman's engraving of the Opie portrait of Foot shows him with wild disheveled hair and a definite exophthalmos. The only public comment that Hunter ever made in regard to Foot was, "Jesse Foot accuses me of not understanding the dead languages, but I could teach him that on a dead body which he never knew in any language, dead or living." Ottley says, "Hunter was too wise to give consequence to his petty foe by publicly replying to his attacks. But the following comments were written by him on a couple of scraps of paper destined for pipe lights but rescued from the flames by Mr. Clift. "One may well say of Jesse Foot, as we sometimes say of young men, 'it was well their fathers were born before them.' It was well for Jesse Foot that I published my book before he wrote his." Once when a friend asked him what he thought of his enemy, Foot, he replied, "Oh, sir, we all have vermin that live on us."

Martin Van Butchell, the most amazing of all of Hunter's curious assortment of friends, was the son of a tapestry maker to the king, who came from Flanders. Unfortunately, of his early life we know little, except that for some years he studied under both of the Hunters. From 1775 to 1800 his advertisements animated the London press. Many descriptions of his curious house on Mount Street, with great and unintelligible advertisements painted across the front, are to be found. He began life as a dentist and then added truss and garter making to his accomplishments. He also invented many devices, among them a fire extinguisher, cork bottoms to stirrups, spring girths for saddles, and rubber tires for carriages. Finally he became a specialist in the treatment of fistula in ano. His son, the first surgeon in England to be sued for malpractice on the death of a patient, followed his father in this specialty. The senior Van Butchell became tremendously upset in his latter days by the fact that the men in England were not permitting their beards to grow. To this practice he allotted the pusillanimity of the race, citing the story of Samson and Delilah for confirmation. It was his habit to ride about on Sundays, wearing heavy dark rimmed spectacles with his beard trailing toward the ground, on a white pony which he not infrequently decorated with

large splotches of purple paint. In the Rev. Lyson's *Collecteanna* in the British Museum there is a wonderful engraving of this get-up. This clipping from a London paper of 1778 throws some light on this remarkable gentleman:

Mr. Van Butcher, a celebrated dentist had the misfortune about five months ago to lose his wife to whom he had the greatest regard. He sent for Dr. Hunter and his assistant, Mr. Crookshanks, and desired he would embalm her, which they did after an entirely new method invented by Dr. Hunter and made use of in embalming Lady Holland. The bowels were first taken out; the vessels were afterwards emptied as perfectly as possible of the blood which they contained, and injected with the oil of turpentine. After the body was well impregnated with that powerful preservant, a large quantity of red, waxy injection was thrown into the vessels, which entering their minute cavities and distending them gave to the face and other parts of the body a most striking appearance of life. The cavity of the body was filled with various aromatic ingredients and she was decently laid in a very handsome box. Under her there is some powder of the plaster of paris to absorb any moisture that might drain from the embalmed body. In the lid of the box there are glasses over her face and legs. A physician who saw her the other day said that the face of Mrs. Van Butcher is not in the least shrunk, that it is not quite so fair as it was, but that the redness from the injection is very striking and that her legs appear to be perfectly natural. Mr. Van Butcher keeps her constantly in the parlor where he sits, shows her to all his friends when they visit him and says it is the only consolation he has since her death. He feels himself above the prejudices of the vulgar and observed that he never did anything in his life which afforded him more satisfaction. Upon the whole he seems pleased with his sweet, handsome and silent wife. What would our leaders say if this whim should happen to strike those leaders of decorum that govern the world of fashion?

Eighteen years later the following item appears in the St. James Chronicle, October 19, 1796.

Van Butchell—(not willing to be unpleasantly circumstanced and wishing to convince some good minds that they have been misinformed) acquaints the curious, no stranger can see his embalmed wife unless (by a friend personally) introduced to himself any day between 9 and 1, Sundays excepted.

Shortly after this, in his old age he remarried. His second wife very unkindly objected to the presence of her predecessor, whereupon the first Mrs. Van Butchell was placed in the museum of the Royal College of Surgeons to seek everlasting repose. In 1786 Van Butchell did a very wily thing. He had let it be known that he wished to be appointed a dentist to His Majesty, George III. When he found that

his name was not to appear on the forthcoming list of appointees he published this letter in the *Morning Post:*

July, 29, 1786.

The Earl of Salisbury,

My Lord—On the ninth of last November I had the honor of praying your lordship would appoint me dentist to the King.

But now, my Lord, the very pleasing prospect and earnest desire of extensive impartial usefulness to His Majesty's good subjects, makes me humbly hope the King will not call me to that honorable appointment.

I am respectfully, my Lord, your most attentive and obedient servant,

Martin Van Butchell.

Some of his advertisements are really delightful. Let me quote extracts from two of them.

The World, December 20, 1790.

His Serene Highness of Orleans encourages the author more than anyone in Britain, except the discerning John Hunter, Esq., F.R.S., Surgeon General of the Army.

Price four guineas ready cash for Martin Van Butchell's new invented Spring Band Regulator (but not such as the Duke of Orleans had). At home from ten till two. Churls may be so good as to stay away. Venez les Gens de Liberati! Sentir le douceur de grand Liberte! Ici cheze moi. Five brave lads should be fed. Nos enfans bien faits comme les fils d'hercule.

The World, January 15, 1791.

Such ladies as wish to dance, (with ease and grace) at the Ball, which will be at St. James' next Tuesday, are respectfully informed that wearing Martin Van Butchell's New Invented Spring Band Garters (by the King's patent) will help to make them superbly happy.

The Marchioness of Salisbury, the Countess of Aylsbury and divers other ladies, having had these garters many months now can tell their friends how much they like them. John Hunter, Esq., F.R.S., Surgeon extraordinary to His Majesty, has six years used and recommended them.

In scanning the long list of distinguished lecturers who have given the annual Hunterian orations since 1814 one finds, I believe, none whose particular interests were psychiatric. Consequently, although Hunter has been viewed from many angles he has never been presented as a psychiatrist. Perhaps one fears that picturing "The Father of Modern Surgery" as a psychiatrist would too greatly tax the credulity of one's auditors. At any rate, one need not fear so. I have not

analyzed all the writings of Hunter with this end in view, although it would prove a fruitful task. But perhaps one might close this modest contribution to the Johns Hopkins Hunterian celebration by presenting two passages which show the great genius Hunter to have been a very astute observer in the field of human behavior.

In the first edition of *A Treatise on the Venereal Disease* (1786), Hunter begins his chapter on Impotence with "This complaint is by many laid to the charge of Onanism at an early age; how far this is just it will in many cases be difficult to determine; for upon a strict review of this subject, it appears to me to be by far too rare to originate from a practice so general." He continues a little further on, "This I can say with certainty, that many of those who are affected with the complaints in question are miserable from this idea. I am clear in my own mind that the books on this subject have done more harm than good. . . . . Nothing hurts the mind of a man so much as the idea of inability to perform well the duty of the sex. If his scrotum hangs low it makes him miserable."

Much of this material is omitted in the later editions. Joseph Adams, who edited the 1810 edition, tells us that the fact that the sensibilities of many were offended by these passages accounts for their exclusion. Can we not justly claim that Hunter was pointing the way toward the psychiatry as well as the surgery of the future?

In the treatise *On the Blood, Inflammation and Gunshot Wounds* we have the following observation, recorded in a footnote by the editor, Everard Home. We know that it is extremely unlikely that Home had a spark of scientific originality,— he purloined all from his great teacher and brother-in-law. So that we can in justice conclude this observation was really John Hunter's. "It is very curious that the sensation of sinking is very uneasy to most animals. When a person is tossed in a blanket the uncomfortable part is falling down. Take any animal in the hand and raise it up, it is very quiet, but bring it down and it will exert all its power of resistance and every muscle in the body is in action; this is the case with a child as early as its birth." This observation preceded those of the Behaviorists by more than a century.

A CASE OF BUNDLE BRANCH BLOCK CONFIRMED BY PATHOLOGICAL STUDY[1]

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Although the clinical and laboratory diagnosis of bundle branch block is not infrequently made, the cases which have been followed up by pathological study are suprisingly few. The object of this paper is to report a case of this kind.

The changes produced in the galvanometric records by lesions in the left and right branches of the His bundle were first demonstrated experimentally by Eppinger and Rothberger (9), and later confirmed by Rothberger and Winterberg (32). Mathewson (24), two years later, discussed the possibility of such lesions in four clinical cases. In 1914, Carter (3) analyzed the first large series of clinical records and defined the criteria essential for the diagnosis of bundle branch block. Since then many cases have been reported, for example, those by Oppenheimer and his co-workers (25, 26) Cowan and Branwell (8), Hart (14), Herrick and Smith (15), Talley and Reed (38), Willius (45, 46) and others.[3] Most of these are clinical studies. The number of cases which include post-mortem examination is very small.

The first such pathological studies were made by Eppinger and Stoerk (10). They examined post-mortem two cases in which, from the electrocardiographic curves, they had postulated the existence of bundle branch injury. In both instances they found lesions in the suspected branch.

In 1912 Cohn and Lewis (6) reported a case of auricular fibrillation and complete heart block with electrocardiographic curves almost identical with those obtained by Eppinger and Rothberger after cutting both branches of the His bundle. Pathological examination showed complete division of both branches from each other and from the main stem.

[1] Submitted for publication March 7, 1929.

[2] John D. Archbold Fellow in Medicine.

[3] Bishop (1), Goodall (12), Hall (13), Hill (17), Hewlett (16).

In 1914, these authors (7) reported the pathological findings in four cases included in Carter's original series. Although there was considerable myocardial damage, they were unable to demonstrate any correlation between the pathological lesions in the tissues studied histologically and the electrocardiographic curves. However, they emphasized the possibility of functional bundle branch block similar to that proven to be possible in the main stem.[4] Indeed they definitely stated that their failure to find demonstrable pathological changes in no way invalidated the electrocardiographic interpretations.

Two years later Oppenheimer and Rothchild (1916–17) (26, 27) reported a series of cases showing that prolongation and other abnormalities of the QRS complex were associated with grave myocardial and endocardial involvement. At this time, they introduced the conception of arborization block. Their final report included 62 cases with 14 necropsies. In this study the criteria used were not identical with those defined by Carter. Indeed the study was made from the point of view of myocardial and endocardial involvement, especially of the terminal ramifications of the Purkinje system, and not with direct reference to possible lesions in the branches of the bundle. As no careful histological study of the main bundle branches was made,[5] no inference can be drawn as to the presence or absence of such lesions.

Subsequently, Oppenhiemer and Pardee (25) reported two interesting and anomalous cases of bundle branch block. In both instances, one a case of right, the other of left bundle branch block, pathological study revealed lesions only in the branch opposite to that suspected clinically! These are the only two such cases in the literature.

In 1918, Van der Stricht (39) made a careful histological study of one of the cases reported by Carter in his second discussion of bundle branch block. In this instance there was extensive diffuse inflammation throughout the greater part of the specialized tissue. The inflammatory process was most marked in the left branch of the bundle and involved the greater part of the terminal arborization of the Purkinje

[4] Such cases have been reported by Krumbhaar (21) Geraudel and Giroux (11), Hume (18), and Oppenheimer and Williams (28).

[5] In one article (27), they stated that serial sections of the conduction system of one of the cases were being prepared. Unfortunately, I have been unable to locate that final report.

system. Thus there was an apparent correlation between the low voltage curves recorded and a diffuse lesion throughout the terminal arborizations.

In 1916, Blackford and Willius (2) in a report on "Chronic Heart Block" mentioned that in one case a calcified nodule was found in one of the branches of the His bundle. They gave no details whatsoever.

Three years later Willius (45) reported a series of 138 cases of bundle branch block. There were only five necropsies. In all these five cases notes were made on the gross and microscopic appearances of the myocardium and the statement was made that "no definite localizing lesions were found." However, upon closer study one finds that there is no indication that serial sections were made of the main stem or suspected branch in any one of these cases. Indeed no note was made of any section taken from these regions.

Similarly, in the report of Herrick and Smith (15) there were two autopsies, but in neither case was the conduction system examined microscopically. Since it is obvious that microscopic lesions of the bundle branch may exist although no macroscopic lesion is visible, no definite conclusions can be drawn unless the suspected bundle has been examined with serial sections.

Waldrop (40), in 1924, and Kauf (19), in 1926, each reported a case of bundle branch block in which the diagnosis was pathologically confirmed. Waldrop's case deserves special note as it is the first one reported in which the diagnosis of bundle branch block was made first clinically, then confirmed by the electrocardiographic tracing and finally confirmed pathologically. Recently, King (20) has made an extensive study of this subject and has outlined the physical signs essential for the clinical diagnosis of bundle branch block.

In the last few years there has been considerable interest in transient, partial and incomplete bundle branch block. Interesting experimental work has been done by Wilson and Herrmann (44), Smith (35, 36), and Sherf and Shookhoff (33, 34). Clinical cases have been reported by Hart (14), Robinson (30, 31), Wilson and Herrmann (43), Willius and Keith (47), White (41, 42) and others.[6] Naturally, in this group, pathological reports are scarce, partly because many patients recovered

[6] For example, those by Mathewson (24), Malcohm (23), Stenstrom (37), Lutembacher (22), Peterson (29), Herrick and Smith (15).

and partly because the transitory character of the block indicated a functional abnormality rather than a demonstrable pathological lesion. Indeed the only pathological report of such a case was made by von Wyss (48) in 1911. He suggested that certain anomalous ventricular complexes were due to the occasional failure of impulses to be transmitted through the left branch. Subsequent post-mortem examination revealed round-cell infiltration throughout the entire bundle with an intense inflammatory reaction in the left branch and only slight involvement of the right.

Thus, to my knowledge the literature contains only eleven cases of complete bundle branch block and one case of transient bundle branch block that have been followed up by careful pathological study. Five of these showed lesions in the suspected bundle, two in the opposite bundle, and in four there was no correlation between the electrocardiographic curves and the pathological conditions which were found.

In this case, the heart had been preserved in formalin for some time before it was obtained for the study of the bundle. Therefore the tissue was neither as promptly nor as well fixed as is desirable for careful histological work. A block was cut to include the left branch of the His bundle as it emerged into the left ventricle. Another block was taken for examination of the A-V node and main stem. After these blocks had been cut, it was not possible to obtain another one suitable for study of the right branch. The region of the S-A node had been destroyed when the heart was originally opened. Therefore this study includes only the A-V node, main stem, and suspected branch. However, in spite of the incompleteness of the study, the positive findings seem to us of sufficient interest to warrant their report.

SUMMARY OF CLINICAL HISTORY

E. G., colored woman of 40 years, was followed in the Hospital and Medical Dispensary from 1922–1927. The history and physical findings were those characteristic of a long-standing chronic rheumatic infection. Her complaint was always the same—palpitation and shortness of breath, associated with a varying number of additional cardiac symptoms.

The physical findings on all four admissions were essentially the same, and consequently only those of the last admission are given in detail.

This admission was precipitated by the sudden onset of sharp pain in the right upper quadrant which radiated to the umbilicus and the back. She gave an interim history of the usual palpitation and occasional dyspnea, and also of occasional clay-colored stools for the previous six months. In September she had an attack of palpitation lasting only one day. However, it was followed by nausea and vomiting for three days, and a week later by another attack of palpitation. Since then she had not been well. On October 14, she came to the hospital and was immediately admitted to the ward.

Physical examination (Dr. Johnston) showed an obese colored woman lying flat in bed. She was pale, cyanotic, evidently acutely ill, and complaining of abdominal pain. Her temperature was 100.6°F. The heart rate was 160 at the apex, and 92 at the wrist. Her respirations were 26 per minute and there was an expiratory grunt. On examination of the head, the eyes and ears showed nothing remarkable; the teeth were carious; the tonsils were enlarged and ragged. (Tonsillectomy had been strongly urged but never done.) The thyroid isthmus was slightly enlarged. The chest was of normal contour. The breath sounds were suppressed and broncho-vesicular in quality with a tubular whisper below the right scapula. There were râles at both lung bases. The heart was very rapid and totally irregular. The P.M.I. was seen in the 5th interspace, 12.5 cm. from the mid-sternal line. On palpation there was felt a systolic shock at the apex but no thrill. Percussion showed a cardiac dullness of 4 cm. to the right and 13.5 cm. to the left. On auscultation the first sound was sharp, rough, and rather loud and was followed by a systolic murmur heard over the entire precordium and well transmitted to the axilla. At times before a strong beat, there was a suggestion of a presystolic murmur. P_2 was greater than A_2. The pulse was totally irregular; the vessel walls were not thickened; the tension not elevated. The maximum pressure was between 108 and 124, the minimum apparently around 84 mm. Hg. (On previous admissions her pressure levels had varied between 95 and 124 systolic and 66 and 84 diastolic.) The liver was tender and greatly enlarged extending nearly to the umbilicus. A definite fluid wave was obtained. The extremities show some pitting oedema.

Laboratory examination. Blood Count: R.B.C. 3,780,000; W.B.C. 14,700 (on previous admissions it had been between 7,000 and 8,000); Hb. 62 per cent. The differential count showed 78 per cent polymorphonuclear cells and 22 per cent lymphoyctes. (Formerly it had never been remarkable, generally averaging 70 per cent polymorphonuclear cells and 30 per cent lymphocytes.) The vital capacity was about 1,200 cc., *i.e.*, 66 per cent below normal. The urine: Sp. gr. 1030, cloudy and of high color; no sugar; considerable albumin; a few granular casts and, for the first time, many pus cells. On previous entries this had shown no indication of renal damage—albumin had always disappeared during her stay in the hospital. The phthalein varied from 50 to 70 per cent excretion in two hours. The N.P.N. of the blood had shown a slight but gradual rise from 29 mgm. per 100 cc. on the first admission to 32 and then to 38 and finally to 42 on this admission. Creatinine

varied from 1.38 to 2.00 mgm. X-ray of chest revealed nothing unexpected. The electrocardiogram taken the next day showed auricular fibrillation (see Fig. 1).

The impression at this time was rheumatic heart disease, auricular fibrillation and myocardial insufficiency. The signs in the chest were not definite, but possibly indicated patchy consolidation. Cholelithiasis, pulmonary infarct, and coronary occlusion were considered.

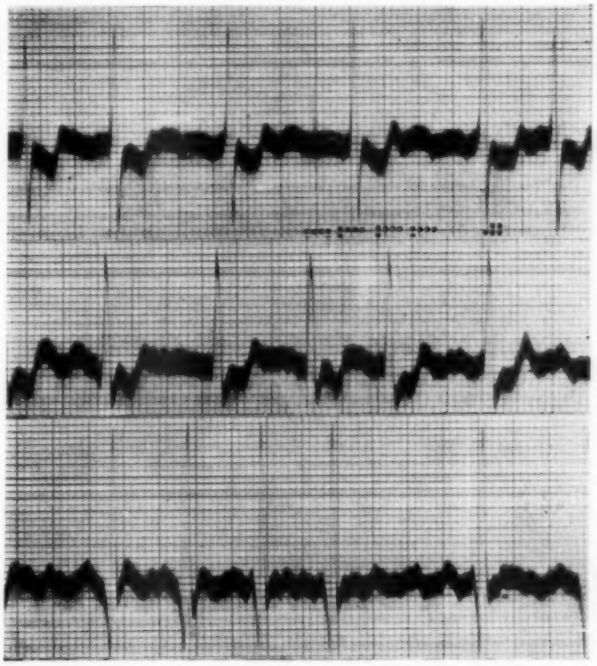

FIG. 1. October 15, 1927. Record shows auricular fibrillation.

Her course in the hospital was rapidly downhill. Her temperature was hectic, varying from 101° to 104°F. The leucocyte count rose steadily, reaching 28,000 on the third day. The heart was weak and totally irregular; under digitalis and other cardiac therapy the rate slowed somewhat and the sounds became definitely louder and the pulse stronger, but in spite of this, the patient grew rapidly worse. She soon became comatose and anuric. By the third day, the N. P. N. had risen, 136 mgm.

The fourth day after admission the patient could not be roused. Her temperature was 105°F. The cardiac rate was rapid (140 at apex) and the rhythm was regular. An electrocardiogram taken at this time (Fig. 2) showed a ventricular tachycardia arising from a focus in the right ventricle with retrograde conduction to the auricles. A few hours later the patient died.

The striking features of this admission were high fever and leucocytosis, and severe myocardial failure without orthopnoea, pulmonary oedema, or engorgement of veins of neck, but with cyanosis, an engorged liver and moderate ascites. The cardiac rhythm was also remarkable in that it changed from auricular fibrillation to a regular but rapid rhythm several hours before death.

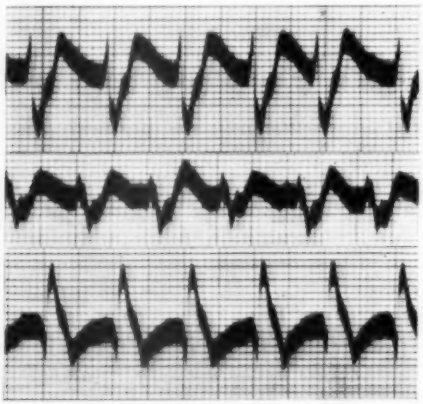

FIG. 2. Record taken a few hours before death, shows ventricular tachycardia arising in the right ventricle with retrograde conduction to the auricle and left bundle branch block.

The clinical impression at the time of autopsy was chronic rheumatic endocarditis and myocarditis; mitral stenosis and insufficiency; myocardial insufficiency and acute cardiac failure.

SUMMARY OF THE POST-MORTEM FINDINGS

The autopsy was done four hours after death by Dr. Margaret Smith.[7] The general picture was that of characteristic long standing chronic passive congestion due to severe myocardial failure.

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[7] I wish to acknowledge my indebtedness for the autopsy report and also for her help in the preparation of normal control sections of the conducting system to Dr. Margaret Smith.

The head revealed nothing abnormal.

The left pleural cavity contained 200 cc. of fluid and there were a few adhesions to the pericardium. The right pleural cavity contained no fluid. There were many fibrous adhesions which partially obliterated this pleural cavity. These had bound the lung to the pericardial sac and to the lower chest wall and diaphragm.

The lungs showed no gross areas of consolidation. Microscopically thrombi of different ages were seen in several of the small arteries.

The abdominal cavity contained a very small amount of free fluid, approximately 100 cc. The liver was enlarged and showed typical chronic passive congestion. The gall-bladder contained a gall-stone 0.5 cm. in diameter. The spleen showed typical chronic passive congestion. The pancreas and adrenals appeared normal. The gastro-intestinal tract and the reproductive organs showed no pathological change.

The kidneys were large, each weighing approximately 220 grams. Both capsules were stripped off with fair ease. On the posterior surface of the left kidney there appeared to be a large fresh infarct; the remainder of the surface showed small haemorrhages and flecks of yellow. On section numerous small infarctions were seen. A few of the small renal arteries were thrombosed but the large renal arteries contained no thrombi, nor did the artery supplying the large area of recent infarction. The right kidney also showed numerous small infarcts of different ages, some old, some fairly recent. The kidney pelves were normal and so were the ureters. The bladder was thickened but otherwise not remarkable. Microscopical examination of the kidneys revealed many infarcts. All the vessels except those in the infarcted areas were normal. There was no thickening about the vessels and no changes were seen in the intima. No bacteria were found in the specially stained sections.

The heart was large. It weighed 690 grams. The pericardium was everywhere adherent to the heart. There were many adhesions to the right lung but not to the anterior chest wall. There was no evidence of a fresh pericarditis. The tricuspid ring measured 9 cm.; its valves were thickened and rolled along their margins. The pulmonary valves were delicate. The pulmonary ring measured 12 cm. The left auricle was very large and the wall thickened. There were no distinct plaques on its wall in the place where a rheumatic process is generally seen. The endocardium was everywhere smooth and glistening. There was a distinct mitral stenosis with great shortening of the chordae tendineae, great thickening of the edge of the valve, and a slight superficial roughening. There was a suggestion of minute grayish vegetations. The mitral ring measured 6 cm. The left ventricle was small compared with the huge right ventricle. The musculature was brown, rather soft, and easily spread apart. One could see no definite suggestion of Aschoff bodies; no nodules could be seen in the musculature even with a hand lens. The aortic valves were just a little stiffened but perfectly competent. The aortic ring measured 7 cm. There was no scarring of the right ventricle. There were no thrombi anywhere in the heart. The coronary vessels were normal.

The routine block for microscopic examination was taken to include a portion of the left auricle, of the left ventricle and of the mitral valve. On section it showed the following: In the auricle there were a few patches of loose connective tissue extending between the muscle cells. These were thought to be the remains of very old scars. At the junction of the mitral valve and the left ventricle there was an area of dense hyaline connective tissue which infiltrated very slightly into the ventricular musculature. The thickened valve was composed of this dense hyaline-like tissue. In the valve there were a few unusually large blood vessels and from its surface protruded several hyaline nodules, presumably old vegetations. In the ventricle were numerous irregular patches of rather fine connective-tissue scarring. No fresh lesions were found. The increase in connective tissue about the blood vessels was inconspicuous. The thickened and adherent pericardium was not shown in the section. However, a small amount of haemorrhage was seen in the fatty sub-epicardial wall.

Smears from the heart's blood and from the cardiac vegetation revealed gram-positive diplococci. The cultures from the heart's blood were negative. None were made from the vegetations.

The aorta showed but a few yellow atheromatous patches consistent with the age of the patient. The microscopic sections showed nothing abnormal.

Special study of the conduction system

A block (0.8 by 1.5 cm.) containing the left branch of the bundle of His was cut from the septal wall of the left ventricle high enough to include the basal attachments of the aortic valve. As the knife was carried across immediately below the right senilunar valve it struck cartilage. This cartilage extended down from the base of the aorta into the septal musculature in the region of the left branch of the His bundle.

The block was fixed in Zenker's, then decalcified with nitric acid, and finally dehydrated in alcohol and embedded in paraffin. Serial sections 7 μ in thickness were cut parallel to the plane of the septal wall. An attempt was made to mount a complete series, but inevitably a few sections were lost. The sections were mounted three on a slide, alternate slides were stained with haematoxylin and eosin, and with phosphotungstic acid haematoxylin.

The portion of the block, composed of the base of the aortic valves and of the cartilaginous area was completely destroyed by the nitric acid. Beneath the margin of the posterior semilunar valve there was a zone of hyalin degeneration in which all cell structure was completely obliterated. This area of degeneration blended with an area of dense connective tissue which was seen to infiltrate between the muscle cells. The muscle fibers, though frequently widely separated from one another by the connective tissue, were well stained by the phosphotungstic acid stain. Even in the places where strands of muscle were buried deep in the connective tissue they stood out a brilliant blue against a background of yellow connective tissue. Throughout this region the blood vessels, wherever visible, appeared to be

normal. Thus the entire process was very similar to that seen at the base of the mitral valve, except that it was much more extensive and became of vital importance because it encroached upon the left branch of the bundle of His.

In order to determine the exact course of the bundle, camera lucida drawings were made. The position of the specialized tissue was carefully plotted on these charts. In this way the course of the bundle could be readily followed. The left

FIG. 3. Slide No. 4 shows specialized tissue as it approaches the scar. Scarcely any specialized tissue is visible beyond the scar.

1, specialized tissue; 2, heart muscle; 3, scar tissue.

branch of the bundle could be seen to emerge between the two cusps along the outer margin of the zone of connective tissue as shown in Figure 3. In places the bundle was apparently pushed laterally and buried in the connective tissue. Some of the cells were greatly distorted; others were markedly compressed. However, there was no absolute break in continuity until the outermost margin of the connective tissue zone was reached. The specialized tissue in this region is shown in Figure 4.

Just at the point where the left branch begins to spread out beneath the endocardium there was a very small but complete break in the continuity of the bundle. Figure 5 shows the specialized tissue just beyond the scarred zone. There was no connection between this part of the conducting system and that shown in the previous section. Beyond this point the amount of specialized tissue increased and could be readily followed as it fanned out beneath the endocardium.

The second block was taken from the interauricular wall of the right auricle. The left lateral margin of the block passed through the coronary sinus. The upper

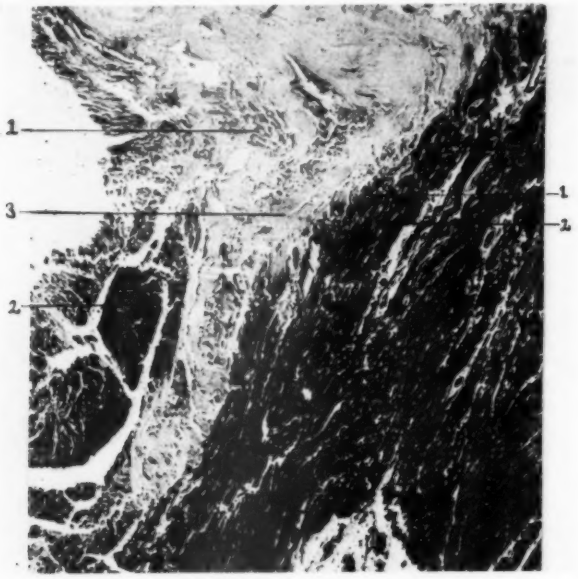

FIG. 4. Slide No. 8 shows a small amount of specialized tissue approaching the scarred area and again a very small amount of specialized tissue is visible beyond the scar.

1, specialized tissue; 2, heart muscle; 3, scar tissue.

border was at the level of the inferior vena cava. The lower extended along the base of the right ventricle until it met the incision of the first block. At this point the right lateral border of the block was cut parallel to the left. This made the block approximately 1.4 cm. square. The thickness of the block was that of the interauricular wall. This piece of tissue was prepared in the same way as the other block. Serial sections, 7 μ in thickness, were made. Every fifth section was mounted and stained with phosphotungstic acid haematoxylin.

These sections showed a large amount of connective tissue in the A-V node and surrounding the main stem. In places the main stem was markedly compressed and its structure was distorted. However, the main stem could be readily traced through the successive sections, showing that there was no demonstrable break in continuity. The vascular supply to this part of the conduction system was extraordinarily rich.

FIG. 5. Slide No. 12 shows a large amount of specialized tissue as it emerges beyond the scar.

1, specialized tissue; 2, heart muscle; 3, scar tissue.

Whether or not the auriculo-nodal junction showed any pathological change is impossible for me to say. Cohn (5) in his study on the auriculo-nodal junction found considerable variation both in the cell structure and in the amount of connective tissue normally present in the A-V node of different hearts. Therefore one must study many sections of this region before one is qualified to judge of possible pathological alterations.

DISCUSSION

The striking clinical features of this case were the persistent cardiac arrhythmias associated with long standing rheumatic heart disease. On virtually every examination, extrasystoles, both auricular and ventricular, were noted unless there was some more serious disturbance in rhythm. In addition to the extrasystoles, the patient was known to have frequent attacks of paroxysmal tachycardia and several attacks of paroxysmal auricular fibrillation. Electrocardiographic records taken during an attack of paroxysmal tachycardia, and several during the periods of auricular fibrillation were especially interesting. The first (Fig. 1), taken the day after admission, showed auricular fibrillation. This persisted until the fourth day when the rhythm was found to be rapid but regular. An electrocardiogram taken at this time showed a ventricular tachycardia arising in the right ventricle with retrograde conduction to the auricle and a left bundle branch block. (See Fig. 2.)

Inasmuch as this is the first and only record in which there was any indication of a bundle branch block, it obviously developed as one of the late manifestations of a long standing cardiac disease. The pathological findings were in apparent accord with these clinical observations. The left branch showed a marked extensive infiltration with connective tissue, which suggested a very old process with a slowly contracting scar. The actual break in the continuity of the bundle was very small indeed. Presumably it was a recent event.

SUMMARY

1. A case is reported in which there was a long standing chronic rheumatic infection with severe myocardial damage. The first definite evidence of left bundle branch block occurred only a few hours before death.

2. Histological examination of the left branch of the His bundle showed extensive scarring, and a very slight actual break in the continuity of the bundle.

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NERVOUS CONTROL OF THE ELECTRICAL RESISTANCE OF THE SKIN[1]

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Experiments reported in previous papers (Richter, '26, '27, '28, '29) have shown how closely the electrical resistance of the skin reflects various changes occurring within the body. It reflects not only simple physiological phenomena, such as the rise and fall of body-temperature and the increased metabolic rate of hyperthyroidism, but also the more complicated psycho-biological changes which take place during normal and pathological sleep, in fear and anxiety states, and in certain types of mental illness, particularly in the catatonic stupors. Therefore, the skin resistance constitutes a simple means for the examination of these different conditions. To understand more clearly the significance of the resistance readings, we have investigated the physiological and neurological factors by which resistance is controlled.

It has been demonstrated that the skin resistance varies in different parts of the body, qualitatively as well as quantitatively. It is lower over areas containing many sweat-glands, such as the palms of the hands and soles of the feet, than over areas with relatively few sweat-glands, such as the dorsal surfaces of the hands and feet; furthermore, it varies independently over these areas, so that the resistance of the skin on the palms may increase while that of the dorsum decreases, and vice versa. Evidence has been presented which indicates that the resistance of the skin on the palm depends on the sweat-glands and is subject to nervous control, while that of the dorsum depends on the epithelial cells and is influenced largely by local conditions. In the present paper a more detailed investigation has been made of the nervous factors involved in the control of skin resistance.

Previous experiments on three monkeys have demonstrated that section of all nerves to the foot produces a very large and apparently

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permanent increase in the electrical resistance of the skin on the sole of the foot (Richter, '26). In one animal the resistance increased from its normal average of 30,000 ohms to 1,780,000, and similar records were obtained on the other two. The skin on the backs of the feet, on the contrary, showed no conductivity changes whatever after complete denervation. These preliminary observations, supported by evidence obtained from injections of atropine and by changes noted during sleep, suggested very strongly that the resistance of the porous skin on the sole of the foot was controlled by nerve impulses, whereas the relatively non-porous skin on the dorsum was subject to other factors. These data served as the starting-point for the present investigation.

Since sectioning the main nerve trunks to the feet severs somatic and sympathetic as well as any para-sympathetic nerves that might innervate the sweat-glands, it was not possible in our preliminary experiments to determine to what extent each of these components might be responsible for the large increase in resistance. In the present experiments an attempt has been made to differentiate the somatic from the sympathetic effects. Inasmuch as nothing is known regarding the anatomical distribution of para-sympathetic nerves to the skin, the rôle played by this component could not be studied experimentally. However, we shall draw attention below to certain indirect evidences of para-sympathetic control of skin resistance.

In one series of experiments the somatic innervation to the feet was removed while the sympathetic remained intact, and in another series the sympathetic innervation was removed while the somatic remained intact. The somatic nerve supply was eliminated by section of the anterior and posterior spinal roots extradurally in the spinal canal. For the denervation of the fore-limbs, C_5 to T_2 were cut; for the hind-limbs, L_3 to S_2. In this way both the sympathetic impulses to the fore-foot, which leave the cord below T_2, and those to the hind-foot, which leave the cord above L_4, were not interrupted. The sympathetic supply to the fore-limbs was eliminated by the removal of the stellate and the first thoracic ganglia; to the hind-limbs, by the avulsion of the sympathetic chain from L_2 to S_2. In these operations, of course, the somatic supply was uninjured.

As a basis for the present work we have repeated our original experi-

ments (total denervation) in a larger number of animals, and have taken records over longer periods of time after the operation. These experiments have confirmed our previous observations, and have brought out a number of additional facts which were not taken into consideration at that time. We shall endeavor to show below to what extent the skin resistance is controlled by the sympathetic and somatic nervous systems, and to what extent these facts may be of value for clinical examination of certain neurological disturbances.

METHODS

The skin resistance was measured by our usual method, described in detail elsewhere (Richter, '27, '29). The non-polarizable electrodes used consisted of sheets of zinc about 1 cm. square and a paste mixture of kaolin and saturated zinc-sulphate solution. A very small constant current was passed through the body and the resistance was measured by means of a string galvanometer.

It is important to mention again in this connection that we measured separately the skin resistance of the soles and backs of the feet on each side of the body. This made it possible to compare at all times the skin resistance on the side of the experimental lesion with that on the normal, uninjured side (Richter, '27). Daily records were taken on most of the animals for at least two weeks before the operation and then for varying intervals up to a year afterwards.

Seven monkeys (*Macacus rhesus*) and seven cats were used in these experiments. Various methods were employed to restrain the animals while the electrodes were being attached and the resistance readings taken. It is difficult to keep the animals from shaking the electrodes from their feet and from putting them into their mouths, etc. To avoid these difficulties in our early experiments we used the following technique. An assistant held the monkey on a pillow in her lap, keeping his fore-limbs behind his back with one hand and his hind-limbs in an extended position with the other hand. This method was not practical for work with cats, however, because of their different anatomical structure. We have recently found a much better method in that it works equally well for cats, dogs, or monkeys. We now put the animal's head in a restraining yoke of the type shown in Figure 1, and the legs are held with little difficulty by an assistant.

Monkeys are most satisfactory for these experiments because their feet are very similar to the human hand in the general shape, in the structure of the skin, and in the comparative absence of hair on the dorsal surfaces. Because of the quantity of hair present on the backs of the cats' feet, it was not possible to make a satisfactory adjustment of the electrodes. The kaolin paste could not be brought into direct contact with the skin unless the hair had been clipped and shaved. In the process of shaving, the skin was always cut in numerous places,

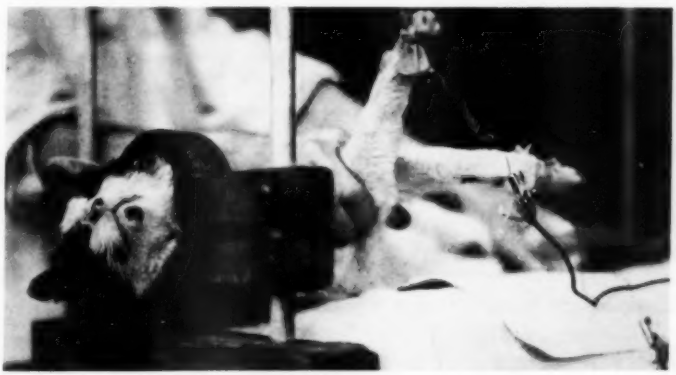


FIG. 1. FRAME USED FOR HOLDING THE ANIMALS WHILE THE RECORDS WERE BEING TAKEN

It works equally well for cats, dogs, and monkeys and can be adjusted to animals of widely different sizes. The frame was designed by Dr. S. S. Tower of the Anatomy Department, Johns Hopkins Medical School.

and this type of injury, as we have shown in previous papers, entirely eliminates the skin resistance. In the cats, therefore, no records have been made of the resistance of the skin on the dorsum of the foot. In the monkey the small amount of hair on the backs of the feet was clipped away with a pair of scissors without any injury to the skin and the electrodes were attached in much the same way as they are attached to the hands of man. One electrode was applied to the sole and one to the back of the foot and the pair were held in place by a piece of cotton padding, 2 cm. wide, wrapped around the foot, and a strip of thin rubber-dam tied around the padding.

A slightly different method was used in attaching the electrodes to the feet of the cats. Because of the peculiar conformation of the sole of the feet and the difficulty of keeping the kaolin paste confined to the pads, the central and largest pad was isolated by means of a piece of rubber-dam in which a hole had been cut just large enough to permit its insertion. In this way the paste from the electrodes touched only the porous pad and was insulated from the very differently constructed non-porous skin surrounding it. The electrode was held in place by means of a second piece of rubber-dam tied around the foot.

We used a modified technique for the cats to measure separately the resistance of the pads on the two sides of the body. Instead of calculating the resistance, as we did in monkeys and man, from the six equations obtained by passing the current by various routes between the two plantar and two dorsal surfaces of the fore and hind-feet, we were able to calculate it very simply by means of one reading. We know that when a current is passed through the body from one part to another, the resistance reading obtained represents the total resistance of the two areas of skin over which the electrodes are attached. If a puncture is made under one electrode, then the remaining resistance is localized in the skin under the other electrode. In this way the resistance can be measured for any area of skin. In the cats, after the electrodes were attached to the pads of the two fore or hind-feet, a third electrode was attached to the pinna of one ear, over a puncture made previously in the skin. The resistance of the skin under the electrode on the ear was thus reduced to zero, and the remaining resistance to a current passing from a pad to the ear was localized in the skin of the pad. In this way it was possible to measure very simply and easily the resistance of the pad on each foot.

The nature of the work made it possible to perform several different operations on each animal, since one animal could be used for two sympathectomy experiments, one of the fore and one of the hind-legs, and two total denervation experiments of the remaining limbs.

RESULTS

Effect produced on skin resistance by section of all nerves, somatic and sympathetic. In this series of experiments the brachial plexus was cut in four monkeys and the sciatic and femoral nerves in three. The

brachial plexus was reached through an incision made in the axilla with the fore-limb fully extended above the animal's head. The sciatic was cut between the biceps femoris and the tractus iliotibialis muscles in the thigh and the femoral nerves in the inguinal region.

A fairly typical record is presented in Figure 2 to show the effect produced on the resistance of the sole and back of the right hind-foot

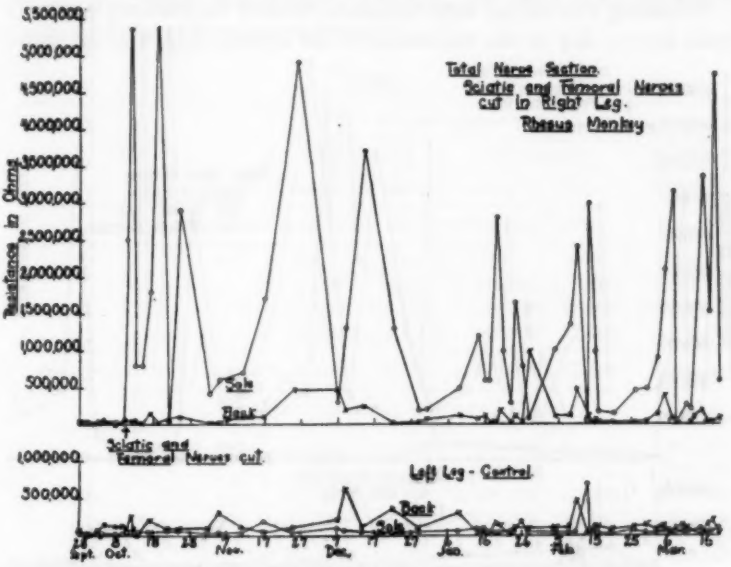


FIG. 2. GRAPH SHOWING THE EFFECT PRODUCED ON THE SKIN RESISTANCE OF A MONKEY BY SECTION OF THE SCIATIC AND FEMORAL NERVES ON THE RIGHT SIDE

The resistance in ohms on the soles and backs of both feet is given on the ordinates, while the duration of the experiment in days is given on the abscissae.

by section of the sciatic and femoral nerves. The resistance of the skin on the sole and back of the left or control foot is also shown in the graph. The resistance in ohms is given on the ordinates and the duration of the experiments in days on the abscissae. Before the operation the average resistance of the right sole was 20,000 ohms; of the right back, 25,000 ohms; of the left sole, 20,000 ohms; and of

the left back, 50,000 ohms. Immediately following the operation the resistance of the right sole increased from 20,000 ohms to 2,500,000, and on the following day to 5,350,000 ohms. The resistance of the right dorsal surface remained unchanged. The resistance of the sole and back of the left foot seemed to be entirely unaffected by the operation.

Following this initial large increase, marked fluctuations occurred from day to day in the resistance of the injured side, and persisted

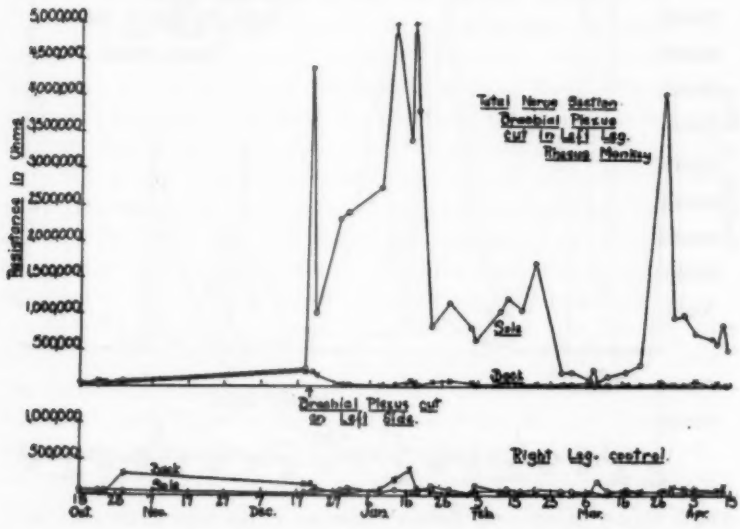


FIG. 3. GRAPH SHOWING THE EFFECT PRODUCED ON THE SKIN RESISTANCE OF THE FORE-FEET BY SECTION OF THE LEFT BRACHIAL PLEXUS

until the experiment was discontinued five months later. There was no tendency, however, for the resistance to return to its original low level; on the contrary, near the end of the five-month period, it almost reached the initial 5,000,000 ohms again. During this entire time the dorsal resistance showed similar slight fluctuations, but these changes were without particular significance since they occurred in like manner on the control side.

The effect produced by section of the brachial plexus in another

monkey is shown in the graph in Figure 3. On the day following the operation on the left leg the resistance of the left sole increased to 4,400,000 ohms, while that of the normal right sole and of both dorsal surfaces was entirely unaffected. There were many fluctuations in the resistance following the initial increase. Twice it rose to 10,794,000 ohms, and at the end of four months it still reached the initial post-operative height occasionally, although for fairly long periods it remained at a comparatively low level.

TABLE I

MONKEY	AVERAGE RESISTANCE				HIGHEST PEAK REACHED ON PLANTAR SURFACE AFTER OPERATION
	Before operation		After operation		
	Plantar	Dorsal	Plantar	Dorsal	
a. Complete transections of sciatic and femoral nerves					
	ohms	*ohms*	*ohms*	*ohms*	*ohms,*
L.	16,000	65,400	1,341,000	122,300	7,190,000
H.	29,000	106,000	2,236,000	87,000	10,794,000
P.	20,700	134,000	645,000	11,000	1,700,000
Average	21,900	101,800	1,407,000	73,400	6,562,000
b. Complete transection of brachial plexus					
L.	27,000	48,000	1,624,000	32,000	10,590,000
S.	6,000	18,000	574,000	8,600	1,500,000
Sl.	15,000	125,000	2,294,000	67,700	5,994,000
P.	18,000	28,000	478,000	15,600	1,200,000
Average	16,500	54,700	1,242,500	30,900	4,872,000

A summary of the results of these operations as given in Table I, shows that the average plantar resistance before the sciatic and femoral nerves were cut was 21,900 ohms. For the entire post-operative period (at least five months) the average was 1,407,000 ohms, and the average highest peak reached was 6,562,000 ohms. The dorsal resistance, on the contrary, decreased slightly—from 101,800 ohms before the operation to 73,400 ohms afterwards. The table shows further that similar changes were produced in the fore-foot by section of the brachial plexus, the plantar resistance increasing from an average of 16,500 ohms to 1,242,500 with an average highest peak of 4,872,000,

and the dorsal resistance decreasing from an average of 54,700 ohms to 30,900.

From these experiments the following conclusions may be drawn. (1) the skin resistance of the porous plantar areas of the feet is controlled to a large extent, but not exclusively, by nerve impulses; (2) the large fluctuations of plantar skin resistance which occur from day to day after total denervation must have a non-nervous origin,—probably local changes in temperature, pressure, etc.; (3) on the basis of these total nerve section experiments it appears that the relatively non-porous areas on the backs of the feet are not controlled by nerve impulses. It will be shown below, however, that actually these areas are under nervous control to some extent.

The effect produced on skin resistance by section of all somatic nerves, leaving the sympathetic nerves intact. The effect produced on skin resistance by section of both the anterior and the posterior spinal roots from C_8 to T_2 was investigated in three monkeys and five cats. The roots were cut extradurally, proximal to the junction of the rami with the main nerve trunk. A single record taken on each of the cats shortly after the operation, and daily records taken on the monkeys for five months afterwards, showed that section of these nerves produces no increase in palmar resistance either immediately or ultimately. These nerves, therefore, obviously have no part in the increased palmar resistance which follows section of the entire peripheral nerve trunk, either the brachial plexus or the sciatic and femoral nerves. On the contrary, the records show that section of the anterior and posterior roots seems to produce a decrease rather than an increase in resistance. In the three monkeys the palmar resistance, which was quite low before the operation, decreased almost to zero afterwards. Attention will be drawn later to the significance of this observation as an indication of a possible participation of the parasympathetic nervous system in the control of skin resistance.

In all of these experiments in which the somatic roots alone were severed, the dorsal skin resistance remained absolutely unaffected, showing merely the usual slight fluctuation which occurred from day to day before the operation.

The effect produced on skin resistance by section of the sympathetic nerves, leaving the somatic nerves intact. In these experiments the

abdominal sympathetic chain was removed in four monkeys, in one on both sides, and the stellate and first thoracic ganglia were removed in six monkeys. The abdominal chain, reached retro-peritoneally through an incision made along the crest of the ileum, was resected from L_2 to S_2. The stellate and first thoracic ganglia were removed either through an opening made in the thorax under artificial respira-

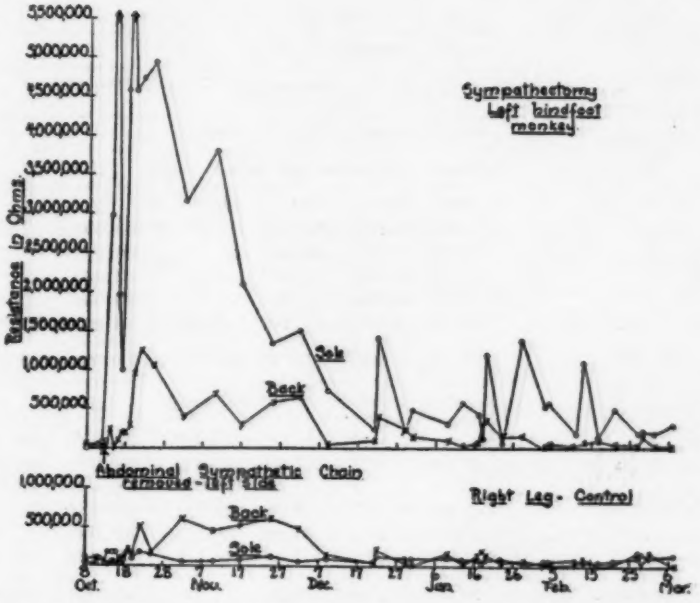


FIG. 4. GRAPH SHOWING THE EFFECT PRODUCED ON THE SKIN RESISTANCE OF THE LEFT HIND-FOOT BY REMOVAL OF THE ABDOMINAL SYMPATHETIC CHAIN FROM L_3 TO S_2

tion, through an opening in the back made by resection of the second and third ribs, or through an incision made in the neck from the tip of the ear ventrally to the sternum.

The effect produced by abdominal sympathectomy in one animal may be seen in Figure 4. The record shows the resistance of both the injured left side and the control right side. Before the sympathec-

tomy the average plantar resistance on the left side was 36,000 ohms, and on the right side 34,000. Immediately following the operation the resistance of the left sole rose to 10,614,000 ohms, while that of the right was unchanged. On the operated side the plantar resistance remained very high for thirty days, and then gradually decreased until, after eighty days, it had reached a fairly permanent average

TABLE II

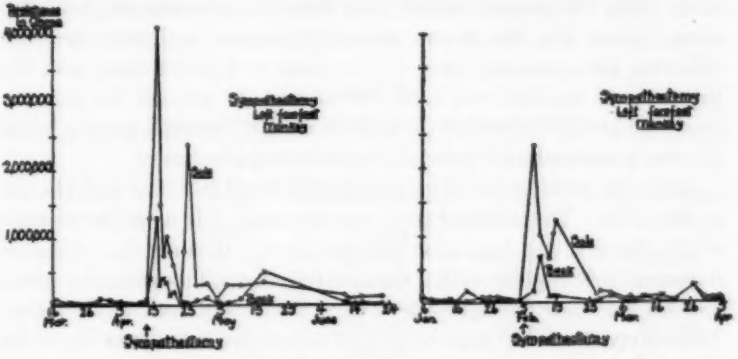
MONKEY	AVERAGE RESISTANCE				HIGHEST POINT REACHED AFTER OPERATION	
	Before operation		For ten days after operation			
	Plantar	Dorsal	Plantar	Dorsal	Plantar	Dorsal
a. Removal of abdominal sympathetic chain						
	ohms	*ohms*	*ohms*	*ohms*		
L. Left	36,000	33,000	4,539,000	415,500	10,614,000	1,250,000
L. Right	60,000	52,000	4,860,000	65,000	7,194,000	200,000
T.	12,700	81,000	1,444,000	314,000	4,554,000	1,650,000
Sl.	8,000	40,000	817,000	71,000	4,104,000	550,000
H.	10,000	18,000	4,476,000	110,000	5,364,000	300,000
Average	25,300	44,800	3,227,200	195,100	6,366,000	790,000
b. Removal of stellate and thoracic ganglia						
S.			156,000	67,000	1,200,000	400,000
H.	24,600	59,000	1,077,000	333,000	1,500,000	800,000
L.	52,000	17,700	1,193,000	337,000	4,200,000	1,300,000
Sl.	12,000	96,000	1,405,000	89,100	5,034,000	500,000
P.	37,500	47,500	183,000	33,600	700,000	110,000
I.	41,300	38,600	1,137,000	179,100	2,300,000	200,000
Average	33,400	51,760	858,500	173,100	2,489,000	551,600

level of 560,000 ohms, in contrast to the original pre-operative average of 36,000 ohms. The highest point reached in this animal, 10,614,000 ohms, is as high as the maximum level reached after section of all nerves to the foot.

It is important to note also that, whereas total nerve section produces no effect on the skin resistance of the backs of the feet, sympathectomy causes a large increase. The dorsal resistance increased on the chart in Figure 4 from a daily average of 36,000 ohms to 1,250,000

on the tenth day after operation. The importance of this increase is somewhat lessened, however, by the fact that the dorsal resistance of the control leg showed a similar smaller increase. After eighty days a final average of 109,000 ohms was reached. This level is also considerably higher than the pre-operative average of 36,000 ohms.

The conductivity changes noted in four monkeys following abdominal sympathectomies, three unilateral and one bi-lateral, are summarized in Table II. The figures there represent the average resistance of the soles and backs of the feet before operation and for a period of ten days thereafter, together with the highest points reached



FIGS. 5A AND 5B. GRAPHS SHOWING THE EFFECT PRODUCED ON THE SKIN RESISTANCE OF THE FORE-FOOT BY REMOVAL OF THE THORACIC CHAIN AND STELLATE GANGLION

by both the soles and backs at any time. The plantar resistance rose from an average of 25,300 ohms before the operation to 3,227,200 ohms afterwards, with an average highest point of 6,366,000 ohms. The dorsal resistance increased from a pre-operative level of 44,800 ohms to 195,100, with an average highest peak of 790,000.

Similar records were obtained by removal of the stellate and the first thoracic sympathetic ganglia. The initial post-operative level of 4,000,000 ohms seen in Figure 5a is as high as that found in some of the abdominal sympathectomy and the total nerve section experiments. The large increase persists for a relatively shorter interval of fourteen days, however, and the final level is not so great as that obtained after

abdominal sympathectomy. The graph shows further that the resistance of the skin on the back of the foot also rose temporarily above the pre-operative average, reaching the highest point, 1,300,000 ohms, two days after the operation and returning to the low pre-operative level ten days later. A similar record is shown in Figure 5b.

The results of these experiments on the removal of the stellate and thoracic ganglia are summarized in Table IIb. The plantar resistance of the five animals rose from the pre-operative average of 33,400 ohms to an average of 858,500 ohms for the ten days after the operation. The highest peak reached by any animal afterward was 5,034,000 ohms, while the average highest peak for the six animals was 2,489,000 ohms. Here also the dorsal resistance showed a definite increase following the operation, from 51,760 ohms to 173,100 ohms, and the highest peak reached was 1,300,000 ohms. In general the increase produced by the removal of the stellate and first thoracic ganglia is not so great as that which follows abdominal sympathectomy.

Attention must be called to several additional facts not brought out in the table. The maximal peak was not reached in all of the animals within the first ten days after the operation. In some the resistance increased only slightly within the first few days after sympathectomy, and did not reach the highest level until the fifteenth or twentieth day. There were also fairly large individual differences in the duration of the effect. In the records of some of the animals (*e.g.*, Fig. 4), the resistance did not return to a lower level until fifty days after the operation, while in others it returned within the first ten days. There were marked differences here between the fore and hind-feet; the effect did not last more than twenty-five days after sympathectomy of the fore-legs, whereas it persisted in some instances for an interval of fifty days in the hind-legs. Furthermore, the final, relatively permanent post-operative level was higher in the hind than in the fore-limbs. The height of the final level usually depended on the magnitude and duration of the initial effect produced by the operation. When the initial increase was very large and prolonged, the final level was always high. The curves fluctuated considerably from day to day for the first ten days after the operation. After this, the fluctuations gradually became less marked, until they finally disappeared altogether. In this respect these curves contrast very sharply with those obtained after section of all the nerves to the feet.

An increase in skin resistance was also produced by sympathectomy in cats. Through the kindness of Dr. S. W. Britton we were able to obtain records on six cats from which the sympathetic chain had been completely removed on one side from just above the stellate ganglion to the point where the chains join in the sacral region. A single record was taken on each animal, about two months after the operation; the results of these measurements are shown in Table III.

The resistance was much higher on the injured side in all but two of the animals. In cat no. 3, the resistance of the operated hind-foot was lower than the control foot, despite the fact that the operated fore-foot showed a higher resistance than the control. Also, in cat no. 9 the resistance was equal on the two fore-feet, although it was

TABLE III

Skin resistance in ohms two months after sympathectomy

CAT	FORE-LIMBS		HIND-LIMBS	
	Normal	Sympathectomized	Normal	Sympathectomized
1	30,000	750,000		
2	30,000	900,000	60,000	300,000
3	12,000	108,000	48,000	13,000
5	30,000	78,000	12,000	35,000
6	34,000	270,000	18,000	60,000
7	32,000	60,000		
9	32,000	32,000	10,000	258,000

higher on the injured hind-foot than on the normal side. These inconsistencies are probably due to the fact that the records were taken two months after the operations, when the resistance had already returned to the lower level at which the differences are not so great. At this point the daily fluctuation might easily result in an occasional higher resistance reading on the normal side. For this reason when resistance records were taken on patients with long-standing lesions of the sympathetic chain it was necessary to make readings on several successive days in order to establish the presence of a higher resistance on the injured side (Richter, '28).

The results of the sympathectomy experiments can be summarized as follows: Sympathectomy produces an initial large increase in the

resistance of the porous areas of the skin of the same magnitude as that which results from section of all the nerves. This large increase is not permanent, however, since after varying intervals (from a few days to three months) the resistance decreases to a much lower level. This level, which is higher in the hind-limbs than in the fore-limbs, appears to be permanent. Finally, sympathectomy causes an increase of conductivity in the relatively non-porous skin on the back of the foot, a fact which demonstrates that the resistance of these areas is not entirely independent of nerve impulses, as the total nerve section experiments seemed to indicate.

The sympathectomy performed in these experiments involved the complete removal of the sympathetic ganglia. In a later paper we shall compare these results with records from animals in which only the pathways between the central nervous system and the ganglia are interrupted, while the ganglia themselves are left untouched. In this way we may determine definitely to what extent the ganglia are capable of autonomous activity.

DISCUSSION

One of the most difficult points to explain in the above data is the fact that after sympathectomy the resistance gradually returns to a lower level again, while after total nerve section the effect is permanent. The most obvious suggestion is that the sympathetic chain regenerates, and the gradual decrease in resistance over a prolonged interval of 20 to 80 days in some animals would favor this theory. In some instances, however, the final level was reached in ten days, so that the time was too short for regeneration. Moreover, since the ganglia were removed in every case, regeneration would be unlikely or impossible according to our present knowledge. Conclusive negative evidence was finally obtained at autopsy when no trace of regeneration could be found.

It seems more likely that the difference was due to the fact that after sympathectomy alone the muscles were still active, and the tissues of the leg were kept in a normal trophic condition with normal metabolism, temperature, etc. It is difficult, however, to accept this view also, for if normal activity of the muscles is the controlling factor, then we might expect the resistance to decrease to its final

level immediately after the operation. A new state of nervous equilibrium must be established gradually in some way after the sympathetic component is removed. Whether this is achieved locally through the development of a semi-autonomous activity of the sweat-glands under the control of inherent nerve elements similar to the enteric plexus of the stomach, or whether through a change in impulses possibly of para-sympathetic origin carried in the spinal nerves, could not be determined.

These experiments have shown very definitely that the usual low level of skin resistance is maintained through the activity of the sympathetic nervous system, since section of the sympathetic nerves causes a marked increase in conductivity. It could not be determined, however, whether the increase in skin resistance which follows sympathectomy is due to the consequent release of active opposing impulses from the para-sympathetic nervous system, or simply to the removal of the sympathetic impulses so that the high resistance of the inactivated skin becomes apparent. Supporting the latter view we have the fact that total nerve section as well as death are followed by an enormous increase in skin resistance. Supporting the view that the increase is due to an opposing force, we have the three experiments in which section of the somatic roots caused the resistance to decrease practically to zero. Any opposing impulses would necessarily have to flow through spinal roots. Blocking these channels might remove the para-sympathetic impulses leaving the sympathetic in full control and reducing the resistance to its lowest level.

The large conductivity increase which occurs during sleep might also be interpreted as a manifestation of para-sympathetic activity, in keeping with the theories of Hess (1925) and others who regard sleep as a condition in which the para-sympathetic nervous system predominates. In previous papers we have shown that during sleep both in man and in monkeys the palmar skin resistance often reaches a level as high as that obtained after sympathectomy or total nerve section (1,800,000 ohms in one patient). This large increase may be caused by para-sympathetic impulses inhibiting the activity of the sweat-glands.

REMARKS

In this, as in most of our previous work, the emphasis was placed on the more or less permanent levels of skin resistance, rather than on the short, transient changes known as the "psychogalvanic reflex." These two phenomena undoubtedly are related, but at present, to make investigation simpler, it seems better to deal with them separately. Nevertheless, it is important to note at this point that the psychogalvanic reflex apparently can be interpreted neurologically as a response to impulses from the sympathetic nervous system. The ingenious experiments of Schilf and Schuberth (1922) on frogs have proved this conclusively. These workers completely severed the body of the frog, anterior from posterior half, except for the sympathetic chain. They then found that nocuous stimulation applied to the head caused the usual reflex decrease in skin resistance in the hind-feet. Inasmuch as the sympathetic chain was the only remaining connection between the two halves of the body, the point was firmly established that these reflex responses arise from impulses passing over sympathetic nerves.

We have been able to confirm these observations of Schilf and Schuberth by records on a patient with a unilateral lesion of the sympathetic chain near the level of the second thoracic ganglion. The psychogalvanic reflex, although very active on the normal side, was entirely lacking on the side of the lesion.

There seems to be little doubt, then, that these transitory changes in resistance depend on the sympathetic nervous system. In the case of the permanent levels of resistance, however, the situation is not so simple, since obviously other factors besides the sympathetic nervous system must be taken into consideration.

CLINICAL APPLICATION

Clinical application of skin resistance methods in the examination of neuro-pathological conditions will necessarily be rather limited until we have established definitely how the skin resistance is influenced, not only by the peripheral part of the sympathetic system, but also by the activity of the cells in the cord and brain. Minor (1923) has shown, however, that in patients with unilateral lesions of the

cervical sympathetic chain the skin resistance on the forehead is higher on the side of the lesion. He thinks, therefore, that the higher skin resistance should be included with the contracted pupil, enophthalmos, and ptosis as a clinical sign of a cervical sympathetic lesion. In the aforementioned patient with a unilateral lesion of the thoracic sympathetic chain, (and a unilateral psychogalvanic response), we found likewise that the resistance was somewhat higher on the side of the lesion, but, as in Minor's records, the difference was not very great. This was undoubtedly due to the fact that the injury to the sympathetic chain had occurred at least several months before and the resistance had already decreased to the final level. The foregoing experiments on monkeys and cats clearly indicate that the significance of clinical records on man would depend to a great extent on the time which had elapsed since the onset of the pathological condition.

From observations made on narcoleptic and encephalitic patients we know that the lesions or functional changes in the sympathetic cells in the region of the third ventricle also produce an increase in skin resistance, but an increase which is not comparable to that produced by lesions of the peripheral mechanism. In five patients who showed both cataplexy and the periodic uncontrollable sleep attacks, the daily palmar skin resistance readings taken when the patients were awake were found to be considerably higher than in waking normals. Several other patients with histories of probable encephalitis some time before our examination also showed skin resistance readings which were higher than any found in normal subjects (Richter, 1928).

CONCLUSIONS

1. Section of all nerves to the feet in monkeys produces an enormous increase in the skin resistance of the plantar areas, containing many sweat-glands, but has no effect on that of the backs of the feet containing relatively few sweat-glands.

2. The increase in the plantar resistance produced in this way seems to be permanent, since it has been found to persist for more than a year after the operation.

3. The increased resistance is not maintained at a constant level but fluctuates markedly from day to day. The cause of the fluctuation is

not known but it is suggested that local changes of pressure, temperature, etc., in the skin may account for it.

4. The somatic nerves do not keep the resistance at its normal low level, since it does not change when these nerves are cut without injury to the sympathetic supply.

5. Removal of only the sympathetic supply to the extremities produces an increase in plantar resistance of approximately the same amplitude as section of the entire nerve trunk.

6. The increase is not permanent, however, as it is after section of all nerves to the legs. It persisted in several animals for twenty days; in others, for only a few days. After this, the resistance decreased to an apparently permanent level, much lower than the original post-operative height, but still considerably above the normal.

7. Various possible explanations were given for the fact that after sympathectomy the large increase is not permanent, while after complete nerve section it is. Regeneration of the sympathetic chain was eliminated chiefly by autopsy findings. It seemed most plausible that the difference arose through the muscular activity still present in the sympathectomized limbs.

8. In all of these experiments except one the lesions were unilateral, so that it was possible to use the other side of the body as a control.

9. The relation of these findings to clinical observations made on patients is discussed.

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